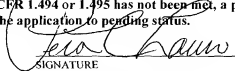


FORM PTO-1500 (REV 10-2000)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER GIN-6718CP5US
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C.371			U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 097743247
INTERNATIONAL APPLICATION PCT/JP99/03929	INTERNATIONAL FILING DATE 22 July 1999 (22.07.99)	PRIORITY DATE CLAIMED 24 July 1998 (24.07.98)	
TITLE OF INVENTION HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS			
APPLICANT(S) FOR DO/EO/US Seishi KATO and Tomoko KIMURA			
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:			
<ol style="list-style-type: none"> <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C.371. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. <input type="checkbox"/> This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)). <input checked="" type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (PCT Article 31). <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) <ol style="list-style-type: none"> <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau). <input checked="" type="checkbox"/> has been communicated by the International Bureau. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C 371(c)(2)). <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) <ol style="list-style-type: none"> <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). <input type="checkbox"/> have been communicated by the International Bureau. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. <input checked="" type="checkbox"/> have not been made and will not be made. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). 			
Items 11. to 16. below concern document(s) or information included:			
<ol style="list-style-type: none"> <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included <input type="checkbox"/> A FIRST preliminary amendment. <ol style="list-style-type: none"> <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. <input type="checkbox"/> A substitute specification. <input type="checkbox"/> A change of power of attorney and/or address letter. <input checked="" type="checkbox"/> Other items or information: Transmittal Letter (2 sheets in duplicate); PCT Request and Fee Calculation Sheet (6 sheets); PCT Notification of Receipt of Record Copy (Form PCT/IB/301) (3 sheets); PCT Notification of Receipt of Search Copy (1 sheet); PCT Notification Concerning Submission of Priority Document (JP 10/208820 filed 24 July 1998) (PCT/IB/304) (1 sheet); PCT International Published Application (WO 00/05367) (without International Search Report) (351 sheets); Cover of PCT International Published Application (WO 00/05367) (with International Search Report attached) (12 sheets); PCT Notification of Transmittal of the International Search Report or the Declaration (14 sheets); PCT Notice Informing the Applicant of the Communication of the International Application to the Designated Offices (PCT/IB/308) (1 sheet); PCT Information Concerning Elected Offices Notified of their Election (PCT/IB/332) (1 sheet); PCT Notification of Receipt of Demand by Competent International Preliminary Examining Authority (1 sheet); PCT Written Opinion (NO RESPONSE NECESSARY) (4 sheets); Notification of Transmittal of the International Preliminary Examination Report (6 sheets); Check (#040892) (\$1130) based on large entity; Certificate of Express Mailing (1 sheet); and Return Postcard. 			

U.S. APPLICATION NO. (if known, see 37 CFR 2.5) 09/743247	INTERNATIONAL APPLICATION NO. PCT/JP99/03929	ATTORNEY'S DOCKET NO. GIN-6718CP5US
17. <input checked="" type="checkbox"/> The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) .(a/o November 1, 2000): Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO..... \$1000 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$860 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.455(a)(2)) paid to USPTO \$710 International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4)..... \$690 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4)..... \$100 <div style="text-align: right;">ENTER APPROPRIATE BASIC FEE AMOUNT =</div>		CALCULATIONS PTO USE ONLY <div style="text-align: right;">\$860</div>
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).		\$--
CLAIMS	NUMBER FILED	NUMBER EXTRA
Total claims	10 -20 =	0
Independent claims	2 -3 =	0
MULTIPLE DEPENDENT CLAIM(S) (if applicable)		+ 270.00
TOTAL OF ABOVE CALCULATIONS =		\$1130
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.		\$--
SUBTOTAL =		\$1130
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).		\$--
TOTAL NATIONAL FEE =		\$1130
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property		\$--
TOTAL FEES ENCLOSED =		\$1130
a. <input checked="" type="checkbox"/> A check (#040892) in the amount of \$1130 to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 12-0080 A duplicate copy of this sheet is enclosed.		Amount to be: refunded \$ charged \$
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.		
SEND ALL CORRESPONDENCE TO: Amy E. Mandragouras, Esq. LAHIVE & COCKFIELD, LLP 28 State Street Boston, Massachusetts 02109 United States of America (617)227-7400 Date: 05 January 2001		
<div style="text-align: center;">  SIGNATURE Peter C. Lauro NAME 32,360 REGISTRATION NUMBER </div>		

DESCRIPTION

Human Proteins Having Hydrophobic
Domains and DNAs Encoding These Proteins

5

TECHNICAL FIELD

The present invention relates to human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies against these proteins. The human cDNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the cDNAs can be utilized as gene sources for large-scale production of the proteins encoded by these cDNAs. Cells into which these genes are introduced to express secretory proteins and membrane proteins in large amounts can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

BACKGROUND ART

Cells secrete many proteins outside the cells. These secretory proteins play important roles for the proliferation control, the differentiation induction, the material transportation, the biological protection, etc. in the cells. Different from intracellular proteins, the secretory proteins exert their actions outside the cells, whereby they can be administered in the intracorporeal manner such as the injection or the drip, so that there are

hidden potentialities as medicines. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents, etc. have been currently employed as medicines. In addition, secretory proteins other than those described above have been undergoing clinical trials to develop as pharmaceuticals. Because it has been conceived that the human cells still produce many unknown secretory proteins, availability of these secretory proteins as well as genes coding for them is expected to lead to development of novel pharmaceuticals utilizing these proteins.

On the other hand, membrane proteins play important roles, as signal receptors, ion channels, transporters, etc. in the material transportation and the information transmission through the cell membrane. Examples thereof include receptors for a variety of cytokines, ion channels for the sodium ion, the potassium ion, the chloride ion, etc., transporters for saccharides and amino acids, and so on, where the genes for many of them have been cloned already. It has been clarified that abnormalities of these membrane proteins are associated with a number of hitherto-cryptogenic diseases. Therefore, discovery of a new membrane protein is anticipated to lead to elucidation of the causes of many diseases, so that isolation of a new gene coding for the membrane protein has been desired.

Heretofore, owing to difficulty in the purification from human cells, these secretory proteins and membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises introduction of a cDNA library into eucaryotic cells to express cDNAs and then screening of the cells secreting, or expressing on the surface of membrane,

the objective active protein. However, this method is applicable only to cloning of a gene for a protein with a known function.

In general, secretory proteins and membrane proteins possess at least one hydrophobic domain inside the proteins, wherein, after synthesis thereof in the ribosome, this domain works as a secretory signal or remains in the phospholipid membrane to be trapped in the membrane. Accordingly, the evidence of this cDNA for encoding a secretory protein and a membrane protein is provided by determination of the whole base sequence of a full-length cDNA followed by detection of highly hydrophobic domain(s) in the amino acid sequence of the protein encoded by this cDNA.

OBJECTS OF THE INVENTION

The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as transformed eucaryotic cells that are capable of expressing these DNAs. This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01550.

Fig. 2 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02593.

Fig. 3 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10195.

Fig. 4 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10423.

Fig. 5 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10506.

5 Fig. 6 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10507.

Fig. 7 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10548.

10 Fig. 8 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10566.

Fig. 9 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10567.

Fig. 10 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10568.

15 Fig. 11 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01426.

Fig. 12 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02515.

20 Fig. 13 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02575.

Fig. 14 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10357.

Fig. 15 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10447.

25 Fig. 16 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10477.

Fig. 17 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10513.

30 Fig. 18 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10540.

Fig. 19 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10557.

Fig. 36 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10530.

Fig. 37 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10541.

5 Fig. 38 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10550.

Fig. 39 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10590.

10 Fig. 40 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10591.

Fig. 41 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01462.

Fig. 42 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02485.

15 Fig. 43 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02798.

Fig. 44 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10041.

20 Fig. 45 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10246.

Fig. 46 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10392.

Fig. 47 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10489.

25 Fig. 48 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10519.

Fig. 49 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10531.

30 Fig. 50 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10574.

SUMMARY OF THE INVENTION

As the result of intensive studies, the present inventors have been successful in cloning of cDNAs coding for proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention.

5 In other words, the present invention provides human proteins having hydrophobic domains, namely proteins comprising any of the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. Moreover, the present invention provides DNAs coding
10 for the above-mentioned proteins, exemplified by cDNAs comprising any of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140, as well as expression vectors that are capable of expressing any of these DNAs by in vitro translation or in
15 eucaryotic cells and transformed eucaryotic cells that are capable of expressing these DNAs and of producing the above-mentioned proteins.

DETAILED DESCRIPTION OF THE INVENTION

20 The proteins of the present invention can be obtained, for example, by a method for isolation from human organs, cell lines, etc., a method for preparation of peptides by the chemical synthesis, or a method for production with the recombinant DNA technology using the DNAs coding for the
25 hydrophobic domains of the present invention, among which the method for production with the recombinant DNA technology is employed preferably. For instance, in vitro expression of the proteins can be achieved by preparation of an RNA by in vitro transcription from a vector having one of
30 the cDNAs of the present invention, followed by in vitro translation using this RNA as a template. Also, introduction of the translated region into a suitable expression vector

by the method known in the art leads to expression of a large amount of the encoded protein in prokaryotic cells such as *Escherichia coli*, *Bacillus subtilis*, etc., and eucaryotic cells such as yeasts, insect cells, mammalian cells, etc.

In the case where one of the proteins of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro, when the translated region of this cDNA is introduced into a vector having an RNA polymerase promoter, followed by addition of the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, containing an RNA polymerase corresponding to the promoter. RNA polymerase promoters are exemplified by T7, T3, SP6, and the like. The vectors containing these RNA polymerase promoters are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II, and so on. Furthermore, the protein of the present invention can be expressed as the secreted form or the form incorporated into the microsome membrane, when a canine pancreas microsome or the like is added to the reaction system.

In the case where one of the protein of the present invention is produced by expressing the DNA in a microorganism such as *Escherichia coli* etc., a recombinant expression vector bearing the translated region of the cDNA of the present invention is constructed in an expression vector having an origin which can be replicated in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator etc. and, after transformation of the host cells with this expression vector, the resulting transformant is incubated, whereby the protein encoded by said cDNA can be produced on a large scale in the

microorganism. In this case, a protein fragment containing any region can be obtained by carrying out the expression with inserting an initiation codon and a termination codon in front of and behind the selected translated region.

- 5 Alternatively, a fusion protein with another protein can be expressed. Only the portion of the protein encoded by this cDNA can be obtained by cleavage of this fusion protein with a suitable protease. The expression vector for *Escherichia coli* is exemplified by the pUC series, pBluescript II, the pET expression system, the pGEX expression system, and so on.

- 10 In the case where one of the proteins of the present invention is produced by expressing the DNA in eucaryotic cells, the protein of the present invention can be produced as a secretory protein or as a membrane protein on the cell-
- 15 membrane surface, when the translated region of this cDNA is introduced into an expression vector for eucaryotic cells that has a promoter, a splicing region, a poly(A) addition site, etc., followed by introduction into the eucaryotic cells. The expression vector is exemplified by pKA1,
- 20 pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, and so on. Examples of eucaryotic cells to be used in general include mammalian cultured cells such as simian kidney cells COS7, Chinese hamster ovary cells CHO, etc., budding yeasts, fission yeasts, silkworm cells,
- 25 *Xenopus* oocytes, and so on, but any eucaryotic cells may be used, provided that they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eucaryotic cells by methods known in the art such as the electroporation method, the calcium
- 30 phosphate method, the liposome method, the DEAE-dextran method, and so on.

After one of the proteins of the present invention is

expressed in prokaryotic cells or eucaryotic cells, the objective protein can be isolated from the culture and purified by a combination of separation procedures known in the art. Such examples include treatment with a denaturing agent such as urea or a detergent, sonication, enzymatic digestion, salting-out or solvent precipitation, dialysis, centrifugation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric focusing, ion-exchange chromatography, hydrophobic chromatography, affinity chromatography, reverse phase chromatography, and so on.

The proteins of the present invention include peptide fragments (5 amino acid residues or more) containing any partial amino acid sequence in the amino acid sequences represented by SEQ ID Nos. 1. to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Hereupon, among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins, after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP 8-187100 A]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secretory forms. Such proteins or peptides in the secretory forms shall come within the scope of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences, expression in appropriate eucaryotic cells affords proteins to which sugar chains are attached. Accordingly, such proteins or peptides to which sugar chains are attached shall come within the

scope of the present invention.

The DNAs of the present invention include all the DNAs coding for the above-mentioned proteins. These DNAs can be obtained by using a method by chemical synthesis, a method
5 by cDNA cloning, and so on.

The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human cells. These cDNAs are synthesized by using as templates poly(A)⁺ RNAs extracted from human cells. The human cells may be
10 cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and
15 Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available, human cDNA libraries can
20 be utilized. Cloning of the cDNAs of the present invention from the cDNA libraries can be carried out by synthesis of an oligonucleotide on the basis of base sequences of any portion in the cDNA of the present invention, followed by screening using this oligonucleotide as the probe according
25 to the colony or plaque hybridization by a method known in the art. In addition, the cDNA fragments of the present invention can be prepared by synthesis of oligonucleotides which hybridize with both termini of the objective cDNA fragment, followed by the usage of these oligonucleotides as
30 the primers for the RT-PCR method using an mRNA isolated from human cells.

The cDNAs of the present invention are characterized by

Table 1

SEQ ID No.	HP number	Cells	Base number	Number of amino acid residues
1, 11, 21	HP01550	Stomach cancer	510	125
2, 12, 22	HP02593	Saos-2	697	131
3, 13, 23	HP10195	HT-1080	1619	242
4, 14, 24	HP10423	U-2 OS	1066	264
5, 15, 25	HP10506	Stomach cancer	618	112
6, 16, 26	HP10507	Stomach cancer	1021	146
7, 17, 27	HP10548	Stomach cancer	1432	344
8, 18, 28	HP10566	Stomach cancer	601	97
9, 19, 29	HP10567	Stomach cancer	585	124
10, 20, 30	HP10569	Stomach cancer	1100	327
31, 41, 51	HP01426	Stomach cancer	1065	313
32, 42, 52	HP02515	Saos-2	937	229
33, 43, 53	HP02575	Saos-2	1578	467
34, 44, 54	HP10357	Stomach cancer	467	99
35, 45, 55	HP10447	Liver	875	189
36, 46, 56	HP10477	Liver	1256	363
37, 47, 57	HP10513	Stomach cancer	884	249
38, 48, 58	HP10540	Saos-2	589	98
39, 49, 59	HP10557	Stomach cancer	673	172
40, 50, 60	HP10563	Saos-2	1425	120
61, 71, 81	HP01467	HT-1080	1436	307
62, 72, 82	HP01956	Liver	997	183
63, 73, 83	HP02545	Saos-2	1753	327
64, 74, 84	HP02551	Saos-2	1117	223
65, 75, 85	HP02631	Saos-2	1380	48
66, 76, 86	HP02632	HT-1080	1503	371
67, 77, 87	HP10488	Liver	733	90
68, 78, 88	HP10538	Saos-2	3768	499
69, 79, 89	HP10542	Stomach cancer	770	106
70, 80, 90	HP10571	Stomach cancer	1229	152

91, 101, 111	HP01470	Stomach cancer	1619	358
92, 102, 112	HP02419	Stomach cancer	2054	226
93, 103, 113	HP02631	Saos-2	1380	195
94, 104, 114	HP02695	Stomach cancer	1292	339
95, 105, 115	HP10031	Saos-2	2168	487
96, 106, 116	HP10530	Saos-2	1357	393
97, 107, 117	HP10541	Stomach cancer	711	196
98, 108, 118	HP10550	Stomach cancer	651	107
99, 109, 119	HP10590	HT-1080	1310	350
100, 110, 120	HP10591	HT-1080	1400	107
121, 131, 141	HP01462	HT-1080	2050	483
122, 132, 142	HP02485	Stomach cancer	2746	334
123, 133, 143	HP02798	HT-1080	1136	267
124, 134, 144	HP10041	Saos-2	619	106
125, 135, 145	HP10246	KB	864	224
126, 136, 146	HP10392	U-2 OS	1527	258
127, 137, 147	HP10489	Stomach cancer	659	110
128, 138, 148	HP10519	Stomach cancer	710	91
129, 139, 149	HP10531	Saos-2	2182	344
130, 140, 150	HP10574	Stomach cancer	2773	428

Hereupon, the same clones as the cDNAs of the present invention can be easily obtained by screening of the cDNA libraries constructed from the human cell lines or human tissues utilized in the present invention by the use of an oligonucleotide probe synthesized on the basis of the cDNA base sequence described in any of SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and 131 to 150.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are inserted, deleted and/or substituted with other nucleotides in SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and

131 to 150 shall come within the scope of the present invention.

In a similar manner, any protein in which one or plural amino acids are inserted, deleted and/or substituted with other amino acids shall come within the scope of the present invention, as far as the protein possesses the activity of any protein having the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

The cDNAs of the present invention include cDNA fragments (10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or in the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Also, DNA fragments consisting of a sense strand and an anti-sense strand shall come within this scope. These DNA fragments can be utilized as the probes for the genetic diagnosis.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant

protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine

levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be

administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium
5 in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation
Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell
10 differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and
15 hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9,
20 B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include
25 without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7,
30 Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular

Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon γ , Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6- Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp.

6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp.

and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

5 Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune
10 thyroiditis, insulin dependent diabetes mellitus, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly
15 allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

20 Using the proteins of the invention it may also be possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by
25 suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing
30 non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent

has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

- 5 Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD).
- 10 For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the
- 15 transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an
- 20 activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen
- 25 function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by
- 30 B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or

tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

5 The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in 10 Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte 15 antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T 20 cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block 25 costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce 30 antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating

autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the commoncold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the

transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

5 In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can
10 be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the
15 expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell.
20 Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary
25 costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected
30 with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and , microglobulin protein or an MHC class

II chain protein and an MHC class II chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J.

Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

- Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.
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- Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.
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- Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965,
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1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

5 Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808,
10 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology
15 1:639-648, 1992.

 Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et
20 al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad. Sci. USA 88:7548-7551, 1991.

Hematopoiesis Regulating Activity

 A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the
25 treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells
30 alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to

stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) 5 useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as 10 thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic 15 utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or 20 ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among 25 other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence 30 embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and

Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

- Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Floemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Tissue Growth Activity

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is

not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and

in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head

trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

5 Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

10 It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including
15 vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

20 A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

25 A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

30 Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon);

International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

- 5 Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Activin/Inhibin Activity

- 10 A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of
- 15 follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals.
- 20 Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- group, may be useful as a fertility inducing therapeutic, based upon the
- 25 ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime
- 30 reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among

other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., *Endocrinology* 91:562-572, 1972; Ling et al., *Nature* 321:779-782, 1986; 5 Vale et al., *Nature* 321:776-779, 1986; Mason et al., *Nature* 318:659-663, 1985; Forage et al., *Proc. Natl. Acad. Sci. USA* 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic 10 or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a 15 desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or 20 neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or 25 indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing 30 such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among

other means, be measured by the following methods:

- Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al. Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

- A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

- The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include,

without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22),

Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A

protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

10 Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of

embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

Examples

The present invention is specifically illustrated in more detail by the following Examples, but Examples are not intended to restrict the present invention. The basic operations with regard to the recombinant DNA and the enzymatic reactions were carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the manufacturer's instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

(1) Selection of cDNAs Encoding Proteins Having Hydrophobic Domains

The cDNA library of fibrosarcoma cell line HT-1080 (WO98/11217), the cDNA library of osteosarcoma cell line Saos-2 (WO97/33993), the cDNA library of osteosarcoma cell line U-2 OS (WO98/21328), the cDNA library of epidermoid

carcinoma cell line KB (WO98/11217), the cDNA library of tissues of stomach cancer delivered by the operation (WO98/21328), the cDNA library of liver tissue delivered by the operation (WO98/21328), and were used for the cDNA libraries. Full-length cDNA clones were selected from respective libraries and the whole base sequences thereof were determined to construct a homo-protein cDNA bank consisting of the full-length cDNA clones. The hydrophobicity/hydrophilicity profiles were determined for the proteins encoded by the full-length cDNA clones registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. Any clone that has a hydrophobic region being putative as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

(2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present invention was used for in vitro transcription/translation with a T₇T rabbit reticulocyte lysate kit (Promega). In this case, [³⁵S]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit. Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25 µl containing 12.5 µl µ of T₇T rabbit reticulocyte lysate, 0.5 µl of a buffer solution (attached to the kit), 2 µl of an amino acid mixture (without methionine), 2 µl of [³⁵S]methionine (Amersham) (0.37 MBq/µl), 0.5 µl of T7 RNA polymerase, and 20 U of RNasin. Also, an experiment in the presence of a membrane system was carried

out by adding to this reaction system 2.5 μ l of a canine pancreas microsome fraction (Promega). To 3 μ l of the resulting reaction solution was added 2 μ l of the SDS sampling buffer (125 mM Tris-hydrochloric acid buffer, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting mixture was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of the translation product was determined by carrying out the autoradiography.

(3) Expression by COS7

Escherichia coli cells bearing the expression vector for the protein of the present invention was incubated at 37°C for 2 hours in 2 ml of the 2xYT culture medium containing 100 μ g/ml of ampicillin, the helper phage M13K07 (50 μ l) was added, and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100 μ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TE).

The cultured cells derived from simian kidney, COS7, were incubated at 37°C in the presence of 5% CO₂ in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% fetal calf serum. Into a 6-well plate (Nunc, well diameter: 3 cm) were inoculated with 1×10^5 COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO₂. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TDMEM). To the resulting cells was added a suspension of 1 μ l of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3 μ l of

TRANSFECTAM™ (IBF) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO₂. After the sample solution was removed, the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO₂. After the culture medium was replaced by a culture medium containing [³⁵S]cystine or [³⁵S]methionine, the incubation was carried out for one hour. After the culture medium and the cells were separated by centrifugation, proteins in the culture medium fraction and the cell-membrane fraction were subjected to SDS-PAGE.

(4) Clone Examples

<HP01550> (SEQ ID Nos. 1, 11, and 21)

Determination of the whole base sequence of the cDNA insert of clone HP01550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 65-bp 5'-untranslated region, a 378-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 125 amino acid residues and there existed one putative transmembrane domain. Figure 1 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 15 kDa that was almost identical with the molecular weight of 13,825 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein F45G2.c (GenBank Accession No. Z93382). Table 2 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C.

elegans hypothetical protein F45G2.c (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.5% in the entire region.

Table 2

10	HP MAKYLAQIIIVMGVQVVGRAFARALRQEF-----AASRAAADARGRAGHRSAAASNLS-
 * * * * * *
	CE MPWRTALKVALAAGEAVAKALTRAVRDEIKQTQQAARHAASTGQSASETRENANSNAKL
	HP GLSLQEAQQILNV-SKLSPEEVQKNYEHLFKVNDSKSVGGSFYLSKVVRAKERLDEEL-K
	* . * . * . * . * . * . * . * . * . * . * . * . * . * . * . * . * . * . *
15	CE GISLEESLQILNVKTPLNREEVEKHVEHLFNINDKSKGGTLYLSKVFRAKERIDEEFGR
	HP IQAQEDREKQMPHT
	* . * . * . * . * . *
	CE IELKEEKKEENAKTE

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA338859) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP02593> (SEQ ID Nos. 2, 12, and 22)

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Determination of the whole base sequence of the cDNA insert of clone HP02593 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 103-bp 5'-untranslated region, a 396-bp ORF,

and a 198-bp 3'-untranslated region. The ORF codes for a protein consisting of 131 amino acid residues and there existed four putative transmembrane domains at the C-terminus. Figure 2 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to a human OB-R gene-related protein (EMBL Accession No. Y12670). Table 3 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human OB-R gene-related protein (OB). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 67.9% in the entire region.

Table 3

HP	MAGIKALISLSPFGGAIGLMFIMLGALPIYNKYWPLFVLFFVILSPIPYCIARRIVDDTD
25	OB MAGVKALVALSFGAIGLTFMLGCALEDYGVYWPLFVLIFHAISPIPHFIKRVTYDSD
HP	AMSACKELAIFLTGTGIVVSAGFLPIVFAHLEIHWGACALVLTGNTVIFATILGFFLVF
	OB ATSSACRELAYFTTGTGIVVSAGFGPVLARVAVIKWGCAGLVLAGNAVIFLTIQGFFLIF
HP	GSNDDFSWQW
30	OB GRGDDFSWEQW

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA306490) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10195> (SEQ ID Nos. 3, 13, and 23)

Determination of the whole base sequence of the cDNA insert of clone HP10195 obtained from cDNA library of human fibrosarcoma HT-1080 revealed the structure consisting of a 286-bp 5'-untranslated region, a 729-bp ORF, and a 604-bp 3'-untranslated region. The ORF codes for a protein consisting of 242 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 3 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was somewhat larger than the molecular weight of 27,300 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein has revealed the registration of sequences that were similar to the Aplysia VAP-33 (SWISS-PROT Accession No. P53173). Table 4 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the Aplysia VAP-33 (AP). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the

present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 46.5% in the entire region.

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Table 4

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HP MAKHEQILVLDPPTDLKFKGPFDDVVTNLKLRNPSPDRKVCVKVKTAPRRYCVRPNSGI
  *.*** *.***.*****.***.***.*****.*****
10 AP MASHEQALILEPAGELRFKGFDDVVTADLKLNPDRRICFKVKTAPKRYCVRPNSGI
HP IDPGSTVTVSVMLQPFDDYDPNEKSKHKFMVQTFAPPNTSD--MEAVWKEAKPDELMDSKL
  ..* .....*****.*****.*** ..* ..* ..* ..* ..* ..*
AP LEPKTSIAVAVMLQPFNYDPNEKNKHKFMVQSMYAPDHVVESQELLWKDAPPESLMDTKL
HP RCVFEMPENNDKLNMEPSK-----AVPLNASKQDGPMPKP--HSVSLNDTE
15 *****..... ..*. ..*.....* ...**..*.....
AP RCVFEMPDPGSHQAPASDASRATDAGAHFSESLEDP TVASRKTETQSPKRVGAVGSAGED
HP TRKLMEECKRLQGEMMKLSEENRHLRDEGLRLRKVAHSD--KPGSTSTASFRDNVTSPLP
  ..** ..* ..* ..* ..*.....*.....* ..* ..*.....
AP VKKLQHELKKAQSEITSLKGENSEQLKDEGIRLRKVAMTDTVSP TPLNPSAPAAA VRAFP
20 HP SLLVVIAAIFIGFGLGKFIL
  ...*.....*.....*
AP PVVYVVAAILGLIGKFL

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25

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA447905) in ESTs, but, since they are partial sequences, it can not be judged whether or not

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any of these sequences codes for the same protein as the protein of the present invention.

<HP10423> (SEQ ID Nos. 4, 14, and 24)

Determination of the whole base sequence of the cDNA insert of clone HP10423 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure consisting of a 64-bp 5'-untranslated region, a 795-bp ORF, and a 207-bp 3'-untranslated region. The ORF codes for a protein consisting of 264 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the N-terminus. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 30 kDa that was almost identical with the molecular weight of 29,377 predicted from the ORF. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D80116) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10506> (SEQ ID Nos. 5, 15, and 25)

Determination of the whole base sequence of the cDNA insert of clone HP10506 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 53-bp 5'-untranslated region, a 339-bp ORF, and a 226-bp 3'-untranslated region. The ORF codes for a protein consisting of 112 amino acid residues and there existed one putative transmembrane domain. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,821 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282544) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10507> (SEQ ID Nos. 6, 16, and 26)

Determination of the whole base sequence of the cDNA insert of clone HP10507 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 412-bp 5'-untranslated region, a 441-bp ORF, and a 168-bp 3'-untranslated region. The ORF codes for a protein consisting of 146 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 16,347 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10548> (SEQ ID Nos. 7, 17, and 27)

Determination of the whole base sequence of the cDNA insert of clone HP10548 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 330-bp 5'-untranslated region, a 1035-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 344 amino acid residues and there existed four putative transmembrane domains. Figure 7 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA143152) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP10566> (SEQ ID Nos. 8, 18, and 28)

Determination of the whole base sequence of the cDNA insert of clone HP10566 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 61-bp 5'-untranslated region, a 294-bp ORF, and a 246-bp 3'-untranslated region. The ORF codes for a protein consisting of 97 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 8 depicts the

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,452 predicted from the ORF. When expressed in COS7 cells, an expression product of about 12 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W79821) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10567> (SEQ ID Nos. 9, 19, and 29)

Determination of the whole base sequence of the cDNA insert of clone HP10567 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 77-bp 5'-untranslated region, a 375-bp ORF, and a 133-bp 3'-untranslated region. The ORF codes for a protein consisting of 124 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 9 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was almost identical with the molecular weight of 14,484 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA428475) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10568> (SEQ ID Nos. 10, 20, and 30)

Determination of the whole base sequence of the cDNA insert of clone HP10568 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 56-bp 5'-untranslated region, a 984-bp ORF, and a 60-bp 3'-untranslated region. The ORF codes for a protein consisting of 327 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36.5 kDa that was almost identical with the molecular weight of 34,326 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Leu-Thr at position 138 and Asn-Leu-Ser at position 206). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from valine at position 24. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the supernatant fraction and the membrane fraction.

30 The search of the protein data base using the amino acid sequence of the present protein has revealed that the protein was similar to the human cell-surface A33 antigen

(SWISS-PROT Accession No. Q99795). Table 5 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human cell-surface A33 antigen (A3). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.0% in the N-terminal region of 243 residues.

Table 5

	HP	MAELPGPF ¹ LCGALLGLCLSGLA ² VEVKV ³ PT ⁴ ELSTPLGKTAELTCTYSTSVGDSFAL-EW
	*.....*.....*.....*
15	A3	MVGKMPVLWLTCAVRVTVDAISVETPQDVLRSQGKSVTLPCYHTSTSSREGLIQW
	HP	SFVQPGKPISESHPILYFTNGHLYPTGSKSKRVLLQNPPTVGVATLKLTDVHPSDGTGY
	 * * * * * * * * * * * * . * * * * *
	A3	DKLL--LTHTERVVIWPF ⁵ SNKN-YIHGELYKNRV ⁶ SISNNAEQSDASITIDQLTMADNGTY
	HP	LCQVNNPPDFYTNGLGLINLTVLVPPSNPLCSQSGQTSVGGSTALRCSSSEGAPKPVYNW
20		* * . . . * * * * * * * * * . * * * * * * * * * *
	A3	ECSVSLMSDLEGNTKSRVRLLVLPSPKPECGIEGETIIGNNIQLTCQSKEGSPTPQYSW
	HP	VRLGTFPTPPSGSMVQDEVSGQLILTNLSLTSSGTYRCVATNQMGASCELTL ⁷ SVTEPS-
		* * * * * * * * * * * * * * * * * * * *
	A3	KRYN ⁸ ILNOEP--LAQPASGQPVSLKNISTDTSGYYICTSSNEEGTQFCNITVAVRSPSM
25	HP	-QGRVAGALIGVLLGVLLLSVA ⁹ AFCLVRFQK ¹⁰ ERGKPK ¹¹ ETYGGSD ¹² LR ¹³ EAT ¹⁴ APGISEPTC
		. . * * . * * *
	A3	NVALYVGIAVGVAALIIIGIIICCCCRGKDNTEDKEDARPNREAYE ¹⁵ EPPEQLRELSR
	HP	MRADSSKGFLE ¹⁶ RPSASTVTTT ¹⁷ SKSLPMV ¹⁸ V
30	A3	EREEEDDYRQEEQRSTGRES ¹⁹ PDHLDQ

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

of sequences that shared a homology of 90% or more (for example, Accession No. T24595) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01426> (SEQ ID Nos. 31, 41, and 51)

Determination of the whole base sequence of the cDNA insert of clone HP01426 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 1-bp 5'-untranslated region, a 942-bp ORF, and a 122-bp 3'-untranslated region. The ORF codes for a protein consisting of 313 amino acid residues and there existed a putative secretory signal. Figure 11 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 34,955 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 38 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ser-Ser at position 163). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from tryptophan at position 17. When expressed in COS7 cells, an expression product of about 39 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R06009) in ESTs, but, since they are
5 partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02515> (SEQ ID Nos. 32, 42, and 52)

10 Determination of the whole base sequence of the cDNA insert of clone HP02515 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 176-bp 5'-untranslated region, a 690-bp ORF, and a 71-bp 3'-untranslated region. The ORF codes for a
15 protein consisting of 229 amino acid residues and there existed a putative secretory signal at N-terminus and one putative transmembrane domain at the C-terminus. Figure 12 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In
20 vitro translation resulted in formation of a translation product of 27 kDa that was almost identical with the molecular weight of 26,000 predicted from the ORF. In this case, the addition of a microsome led to the formation of a
25 product of 25.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from phenylalanine at position 28.

30 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human T1/ST2 receptor binding protein (GenBank Accession No. U41804). Table 7 shows the

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA381943) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02575> (SEQ ID Nos. 33, 43, and 53)

Determination of the whole base sequence of the cDNA insert of clone HP02575 obtained from cDNA library of human osteosarcome cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1404-bp ORF, and a 219-bp 3'-untranslated region. The ORF codes for a protein consisting of 467 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 13 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 52 kDa that was almost identical with the molecular weight of 54,065 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 57 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exist in the amino acid sequence of this protein three sites at which N-glycosylation may occur (Asn-Arg-Thr at position 171, Asn-Ser-Thr at position 239 and Asn-Asp-Thr at position 377). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from histidine at position 29. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the supernatant fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human α -L-fucosidase (SWISS-PROT Accession No. P04066). Table 8 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human α -L-fucosidase (FC). Therein,

[illegible]

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N28668) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10357> (SEQ ID Nos. 34, 44, and 54)

Determination of the whole base sequence of the cDNA insert of clone HP10357 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 113-bp 5'-untranslated region, a 300-bp ORF, and a 54-bp 3'-untranslated region. The ORF codes for a protein consisting of 99 amino acid residues and there existed two putative transmembrane domains. Figure 14 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 11 kDa that was almost identical with the molecular weight of 10,923 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA477156) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10447> (SEQ ID Nos. 35, 45, and 55)

Determination of the whole base sequence of the cDNA

insert of clone HP10447 obtained from cDNA library of human liver revealed the structure consisting of a 271-bp 5'-untranslated region, a 570-bp ORF, and a 34-bp 3'-untranslated region. The ORF codes for a protein consisting of 189 amino acid residues and there existed five putative transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA296976) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10477> (SEQ ID Nos. 36, 46, and 56)

Determination of the whole base sequence of the cDNA insert of clone HP10477 obtained from cDNA library of human liver revealed the structure consisting of a 149-bp 5'-untranslated region, a 1092-bp ORF, and a 15-bp 3'-untranslated region. The ORF codes for a protein consisting of 363 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 16 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,884 predicted from the ORF.

The search of the protein data base using the amino

of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10513> (SEQ ID Nos. 37, 47, and 57)

Determination of the whole base sequence of the cDNA insert of clone HP10513 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 134-bp 5'-untranslated region, a 750-bp ORF, and a 0-bp 3'-untranslated region. The ORF codes for a protein consisting of 249 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 17 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 27,373 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0512 (GenBank Accession No. AB011084). Table 10 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0512 (KI). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 31.6% in the C-terminal region of 196 amino acid residues.

Table 10

```

5      HP      MGGPRGAGWVAAGLLLGAGACYCIYRLTRGRRRG
      KI RGRGRRPVAMQKRPFFPYEIDEILGVRDLRKVLALLQKSDDPFIQQVALLTSLNNANYSCN
      HP DRELGISSKSAEDLTDGSDYDNLVAEQQLLYLLESTEDPVIIRALITLGNNAAFSV
      *      *      *      *      *      *      *      *      *      *
      KI QETIRKLGGLPIIANMINKTDPHIKEKALMAMNLSNENYNGRQLQVYMKNVMDDIMASN
10     HP NQATIRELGGPIIVANKINHSNQSIKEKALNALNLSNVNENQIKIKVQVLKLLNLSEN
      .      .      *      .      .      .      *      .      .      .      *      *      *      *      *
      KI LNSAVQVVGLKFLTNMTITNDYQHLVNSIANF--FRLLSQGGGKIKVEILKILSNFAEN
      HP PAMTEGLLRAQVDSFSLSYDHSVAKIEILLRVLTFLFNKKNCLKIEGHLAVQPTFTEGSL
      *      *      *      *      *      *      *      *      *      *      *      *      *      *      *
15     KI PDLMLKLLSTQVPASFSYLNSYVESEILINALTLFEIYDNLRAE--VFNYREFNKGSL
      HP FFL-LHGECAQKIRALVDHDAEVEKEKVVTTIPIKI
      *      *      *      *      *      *      *      *      *      *
      KI FYLCCTTSKGVCKKIRALANHHDLVLVKVVIKLVNKF

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20 Furthermore, the search of the GenBank using the base
sequences of the present cDNA has revealed the registration
of sequences that shared a homology of 90% or more (for
example, Accession No. N92228) in ESTs, but, since they are
25 partial sequences, it can not be judged whether or not any
of these sequences codes for the same protein as the protein
of the present invention.

<HP10540> (SEQ ID Nos. 38, 48, and 58)

30 Determination of the whole base sequence of the cDNA
insert of clone HP10540 obtained from cDNA library of human
osteosarcoma cell line Saos-2 revealed the structure

consisting of a 47-bp 5'-untranslated region, a 297-bp ORF, and a 245-bp 3'-untranslated region. The ORF codes for a protein consisting of 98 amino acid residues and there existed two putative transmembrane domains. Figure 18 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CEF49C12.12 (GenBank Accession No. Z68227). Table 11 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CEF49C12.12 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 36.1% in the entire region.

Table 11

25	HP M-ASLLCCGPKLAACGIVLSAWGVIMLIMLGIFNVHSAVLIEDVPFTEKDFENGQPNIY
	* *** * * * * * * * * * * * * * *
	CE MGKICPLMGPKMSAFCMVMSVWGVIFLGLLGVFFYIQAVTLFPDLHF-EGHGKVPSSVID
	HP NLYEQVSYNCFIAAGLYLLGGFSFCQVRLNKRKEYMVR
	* * * * * * * * * *
30	CE AKYNEKATQCWIAAGLYAVTLIAVFWQ---NKYNTAQIF

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA420715) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10557> (SEQ ID Nos. 39, 49, and 59)

Determination of the whole base sequence of the cDNA insert of clone HP10557 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 24-bp 5'-untranslated region, a 519-bp ORF, and a 130-bp 3'-untranslated region. The ORF codes for a protein consisting of 172 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 19 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was larger than the molecular weight of 18,844 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 39 kDa which is considered to have been subjected to some modification after secretion. In addition, there exist in the amino acid sequence of this protein no site at which N-glycosylation may occur. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 32. When expressed in COS7 cells, an expression product of about 20 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human progesterone binding protein (EMBL Accession No. AJ002030). Table 12 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human progesterone binding protein (PG). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.5% in the C-terminal region of 151 amino acid residues.

Table 12

15

HP	MVG PAP
PG MAAGDGDVKLGTLGSGSESSNDGGSESPGDAGAAEGGGWAAAAALLTGGGEMLLNVAL HP RRRLRPLAALALVLALAPGLPTARAGQTPRPAERGGPPV--RLFTEELARYGGEEDQPI	
20 ** **..* * * * * PG VALVLLGAYRLWVRWRRGLGAGAGAGEESPATSLPRMKKRFSLQLRQYDG-SRNPRI HP YLAVKGVVFDVTSKGFEYGRGAPYNALTGKDSTRGVAKMSLDPADLTHDTTGLTAKELEA	
.* **.*.....**..*.....*.....* * *	
PG LLAVNGKVFDVTKGSKFYGPAGPYGIFAGR DASRLATFCLDKDALRDEYDDLSDLNAVQ	
25 HP LDEV--FTKVYKAKYPIVGYTARRILNEDGSPNLDKFPEDQPHFDIKDEF	
...* .. .*** ..* * * * * .. . *.....* * ..	
PG MESVREWEMQFKEYK---DYVG-RLKPGEEPS-EYTDEEDTKDHNKQD	

30

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA101709) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5

<HP10563> (SEQ ID Nos. 40, 50, and 60)

Determination of the whole base sequence of the cDNA insert of clone HP10563 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 126-bp 5'-untranslated region, a 363-bp ORF, and a 936-bp 3'-untranslated region. The ORF codes for a protein consisting of 120 amino acid residues and there existed two putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 18.5 kDa that was larger than the molecular weight of 13,180 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein F27F23.15 (GenBank Accession No. AC003058). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the A. thaliana hypothetical protein F27F23.15 (AT). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.5% in the entire region.

The search of the protein data base using the amino

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HP  MSMILSASVIRVRDGLPLSASTDYEQSTGMQECRKFYKMLSRKLAQLPDRCTLKTGHYNI
    *****_*****_*_*****_*****_*****_*_*
RN  MSMILSASVVRVRDGLPLSASTDCEQSAGVQECRKFYKMLSRKLAQFPDRCTLKTGRHN
HP  NFISSLGVSVMMLCTENYPNVLAFSFLDELQKEFITTYNMKMTNTAVRPPYCFIEFDNFQ
    *****_*****_*_*_*****_*****_*****_*_*
RN  NFISSLGVSVMMLCTENYPNVLAFSFLDELQKEFITTYNMKMTNTAVRPPYCFIEFDNFQ
HP  RTKQRYNPNRSLSTKINLSDMQTEIKLRPPYQISMCELGSANGVTSAFSVDCKGAGKISS
    *****_*****_*_*_*****_*****_*****_*_*
RN  RTKQRYNPNRSLSTKINLSDMQMEIKLRPPYQIPMCELGSANGVTSAFSVDCKGAGKISS
HP  AHQRLEPATLSGIVGFILSLLCGALNLIRGFHAIESLLQSDGDDFNXYIAFFLGTAACLY
    *****_*****_*_*_*****_*****_*****_*_*
RN  AHQRLEPATLSGIVAFILSLLCGALNLIRGFHAIESLLQSDGEDFSYIAFFLGTAACLY
HP  QCYLLVYVTGWRNVKSFLTGTLCLCNMYLYELRNLWLQFLPHVTVGAFVTLQWLRLQAQG
    *
RN  QMICLCLOGRKERT

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA421925) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01956> (SEQ ID Nos. 62, 72, and 82)

Determination of the whole base sequence of the cDNA insert of clone HP01956 obtained from cDNA library of human liver revealed the structure consisting of a 86-bp 5'-untranslated region, a 552-bp ORF, and a 359-bp 3'-untranslated region. The ORF codes for a protein consisting of 183 amino acid residues and there existed one putative transmembrane domain. Figure 22 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20.5 kDa that was almost identical with the molecular weight of 20,073 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the yeast hypothetical protein 21.5 kDa (SWISS-PROT Accession No. P53073). Table 15 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the yeast hypothetical protein 21.5 kDa (SC). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology

of 34.3% in the C-terminal region of 108 amino acid residues.

Table 15

5 HP MTAQGGLVANRGRFRKWAIELSGPGGSGRGRSDRSGQGDSLYPVGYLDKQVPDTS

SC MSEQEPYEWAKHLLDTKYIEKYNIQNSNTLPSPPGFEGNSKGNVTRKQDQTSQTSTLA

HP VQETDRILVEKRCWDIALGFLKQIPMNLFIMYMAGNTISIFPTMMVCMMAWRPIQALMAI

 * .. *.*** * * *.***. *.***... *.** * .. **.*....

10 SC QKNQITVLQVQKAWQIALQPAKSIPMNIFMSYMSGTSLQIIPMTALMLLSGPIKAIFST

HP SATFK--MLESSQKFLQGLVYLIGNLMGLALAV-Y-KCQSMGLLPHASDWLAFIEPPE

 *** .. **.*. *.** ... * .. * .. * .. * .. * .. * .. * .. * .. *

SC RSAFKPVLGNKATQSQVQTAMFMYIVFQGLVMIYIGYRKLNSMGLIPNAKGDWLPWERIAH

HP RMEFSGGGLLL

15

SC YNNGLQWFSD

20 Furthermore, the search of the GenBank using the base
 sequences of the present cDNA has revealed the registration
 of sequences that shared a homology of 90% or more (for
 example, Accession No. AA159753) in ESTs, but, since they
 are partial sequences, it can not be judged whether or not
 any of these sequences codes for the same protein as the
 25 protein of the present invention.

<HP02545> (SEQ ID Nos. 63, 73, and 83)

30 Determination of the whole base sequence of the cDNA
 insert of clone HP02545 obtained from cDNA library of human
 osteosarcoma cell line Saos-2 revealed the structure
 consisting of a 133-bp 5'-untranslated region, a 984-bp ORF,
 and a 636-bp 3'-untranslated region. The ORF codes for a

protein consisting of 327 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 23 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the rat embigin (EMBL Accession No. AJ009698). Table 16 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat embigin (RN). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 65.4% in the entire region.

Table 16

[illegible]

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA312629) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02551> (SEQ ID Nos. 64, 74, and 84)

Determination of the whole base sequence of the cDNA insert of clone HP02551 obtained from cDNA library of human

osteosarcoma cell line Saos-2 revealed the structure consisting of a 61-bp 5'-untranslated region, a 672-bp ORF, and a 384-bp 3'-untranslated region. The ORF codes for a protein consisting of 223 amino acid residues and there
5 existed a putative secretory signal at the N-terminus. Figure 24 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was somewhat larger than
10 the molecular weight of 24,555 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 26 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the
15 secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 20.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse FGF binding protein
20 (GenBank Accession No. U49641). Table 17 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse FGF binding protein (MM). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the
25 protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 21.2% in the entire region other than the N-terminal region. In particular, all the eight cysteine residues contained in the
30 both proteins were conserved.

Table 17

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      HP                                     MKFVPCLLLVTLSCGLTGQAAPRQKQGST
                                         ..***. . * . ...
5 MM MRLHSLILLSFLLLQAFSEKVRKRAKNAPHSTAEEGVEGSAPSLSGAQNQRSSRTSKS
HP GEEFHFQTGGRRSCITMRPSSLGQGAGEVWLRVDCRNTDQTYWCEYRGQPMSMCAADPFK
    . * . * . * . * . * . * . * . * . * . * . * . * . * . * . * .
MM LTHGKFVTKDQATC---RWAVTEEEQGISLKVQCTQADQEFSCVFGADPTDCLKHDKD-Q
HP SYWNQALQLRLRHACQGA-PVLRP SVCREAGPQAHMQQVTS SLKGSPEPNQQEAGTP
10 ***. . ** . * . * . * . * . * . * . * . * . * . * . * .
MM IYWQKVARTLRQKNICRDAKSVLKT RVC RKFPESNLKLVNPNARGNTKPRKEAEVSA
HP SLRPKATVKLTEATQLGKDSMEELGKA KPTTRPTAKPT QPGPRPGNEEAKKWEHCWK
    . . . . . * . . . . * . * . * . * . * . * . * . * . * . * .
MM REHNKVQEAVSTEPNR IKEDI-TLNPAATQTM-TIRDPECLEDPDVLNQ-RKTALEFCGE
15 HP PFQALCAFLISFFRG
    . . . *. * . . . .
MM SWSSICTFFLNLMQATSC

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20 Furthermore, the search of the GenBank using the base
sequences of the present cDNA has revealed the registration
of sequences that shared a homology of 90% or more (for
example, Accession No. AA317400) in ESTs, but, since they
are partial sequences, it can not be judged whether or not
25 any of these sequences codes for the same protein as the
protein of the present invention.

<HP02631> (SEQ ID Nos. 65, 75, and 85)

Determination of the whole base sequence of the cDNA
30 insert of clone HP02631 obtained from cDNA library of human
osteosarcoma cell line Saos-2 revealed the structure
consisting of a 42-bp 5'-untranslated region, a 147-bp ORF,

and a 1191-bp 3'-untranslated region. The ORF codes for a protein consisting of 48 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa or less.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA156969) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02632> (SEQ ID Nos. 66, 76, and 86)

Determination of the whole base sequence of the cDNA insert of clone HP02632 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 50-bp 5'-untranslated region, a 1116-bp ORF, and a 337-bp 3'-untranslated region. The ORF codes for a protein consisting of 371 amino acid residues and there existed eight putative transmembrane domains. Figure 26 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELC2H12 (GenBank Accession No. U23169). Table 18 shows the comparison between amino acid sequences

of the human protein of the present invention (HP) and the C. elegans hypothetical protein CELC2H12 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 51.4% in the entire region.

Table 18

10

HP MAWTKYQLFLAGLMLVTGSINTLSAKWADNFMAEGCGSGSKEHSFQHPFLQAVGMFLGEFS
*.*****.*****.....*.....*.....*.....*

CE MVAFVAIISVMVVTGSLNTICAKWADSIKAD-----GVFPNHPFLQATCMFFGEFL

15

HP CLAAFYL-----LRCRAAGQSDS-----SVDPQQPFNPLFLPALCDMTGTSL

***.*.....*.....*.....*.....*.....*.....*.....*

CE CLVVFFLIFGYKRYVWNRANVQGESGSVTEITSEEKPTLPPFNPFLLFPFPALCDILGTSI

HP MYVALNMTSASSFQMLRGAVIIFTGLFSVAFGLGRRLVLSQWLGILATIAGLVVVGGLADLL

***.*.....*.....*.....*.....*.....*.....*.....*

CE MYIGLNLTTASSFQMLRGAVIIFTGLLSVGLMNAQIKPFKWFGLFVMLGLVIVGVTDIY

20

HP SKHDSQHKLSEVITGDLIIIAQIIVAIQMVLEEKFPVKHNVHPLRAVGTEGLFGFVILS

..*.....*.....*.....*.....*.....*.....*.....*

CE YDDDLPLDDKNAIITGNLLIVMAQIIVAIQMVYEQKYLTXYDVPALFAVGLEGLFGMVTLS

HP LLLVPMYYIPAG-SFSGNPRGTLEDALDAFCQVQQPLIAVALLGNISSIAFFNFAGISV

..........*.....*.....*.....*.....*.....*

25

CE ILMIPFFYYIHPRTFTSTNPEGRLEDVFYAWKEITEEPTIALALSGTVSVSIAFFNFAGVSV

HP TKELSATTRMVLDSLRTVVIWALSALGWEAFHALQILGFLILLIGTALYNGLHRPLLGR

*****.*.....*.....*.....*.....*.....*.....*.....*

CE TKELSATTRMVLDSVRTLVIWVVSIPLFHEKFIAIQLSGFAMLIIGTLIYNILIGPWFR

HP LSRGRPLAESESEQERLLGGTRTPINDAS

30

CE RNILPNLSSHANCARCWLCCICGGDSELIEYEQEDQEHLMEA

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N50907) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10488> (SEQ ID Nos. 67, 77, and 87)

Determination of the whole base sequence of the cDNA insert of clone HP10488 obtained from cDNA library of human liver revealed the structure consisting of a 39-bp 5'-untranslated region, a 273-bp ORF, and a 421-bp 3'-untranslated region. The ORF codes for a protein consisting of 90 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 27 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,151 predicted from the ORF. When expressed in COS7 cells, an expression product of about 6 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H73534) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10538> (SEQ ID Nos. 68, 78, and 88)

Determination of the whole base sequence of the cDNA insert of clone HP10538 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 357-bp 5'-untranslated region, a 1500-bp ORF, and a 1911-bp 3'-untranslated region. The ORF codes for a protein consisting of 499 amino acid residues and there existed at least four putative transmembrane domains. Figure 28 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse pore-forming K⁺ channel subunit (GenBank Accession No. AF056492). Table 19 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse pore-forming K⁺ channel subunit (MM). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 32.4% in the N-terminal region of 241 amino acid residues.

Table 19

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5  HP  MVDRGPLLTSIIIFYLAIGAAIFEVLEEPHWKEAKKNYYTQKLHLLEKFPCLGQEGLDK
      * . . . . . * . . . . . * . . . . . * . . . . . * . . . . .
MM  MRSTTLALLLVLLYLVSGALVFOALEQPHEQQAQKMDHGRDQFLRDHPCVSQKSLED
HP  ILEVVSDAAGQG-----VAITGNQTFNNWNWPNAMIFAATVITTIIGYGNVAPKTPAGRLF
      . . . . . * * * . . . . . * . . . . . * . . . . . * . . . . .
MM  FIKLLVEALGGGANPETSWTNSSNHSSAWNLSGAFFFSGTIITTIIGYGNIVLHTDAGRLE
10 HP  CVFYGLFGVPLCLTWISALGKFPGGRAKR----LGQPLTKRGVSLRKAQITCTVIFIVWG
      * . . . . * . . . . * . . . . * . . . . * . . . . *
MM  CIFYALVGIPLFGMLLAGVGDRLGSSLRGIGHIEAIFLKWVPPGLVRSLSAVLFLIG
HP  VLVHLVIPPFVFMVTEGWNYIEGLYSFITISTIGFGDFVAGVNPSANYHALYRYFVELW
      * . . . . * . . . . * . . . . * . . . . * . . . . *
MM  CLLFVLTPTFVFSYMESWSKLEAIYFVIVTLTTVGFGDYVPG-DGTGQNSPAYQPLVWFW
15 HP  IYLGlawLSLFVNWVSMFVEVHKAIKRRRRRRKESFESSPHSRKALQVKGSTASKDVNI
      * . . . . .
MM  ILFGLAYFASVLTTIGNWLRVSRRTAEMGGLTAQAASWTGTVTARVTRTQTCPSAPPE

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20 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R25184) in ESTs, but, since they are partial sequences, it can not be judged whether or not any

25 of these sequences codes for the same protein as the protein of the present invention.

<HP10542> (SEQ ID Nos. 69, 79, and 89)

30 Determination of the whole base sequence of the cDNA insert of clone HP10542 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 23-bp 5'-untranslated region, a 321-bp ORF, and a 426-bp 3'-

untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 29 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,724 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA029683) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10571> (SEQ ID Nos. 70, 80, and 90)

Determination of the whole base sequence of the cDNA insert of clone HP10571 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 95-bp 5'-untranslated region, a 459-bp ORF, and a 675-bp 3'-untranslated region. The ORF codes for a protein consisting of 152 amino acid residues and there existed one putative transmembrane domain. Figure 30 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 20 kDa that was larger than the molecular weight of 17,062 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 23 kDa

which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ile-Thr at position 10).

5 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA105822) in ESTs, but, since they are partial sequences, it can not be judged whether or not
10 any of these sequences codes for the same protein as the protein of the present invention.

<HP01470> (SEQ ID Nos. 91, 101, and 111)

Determination of the whole base sequence of the cDNA
15 insert of clone HP01470 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 157-bp 5'-untranslated region, a 1077-bp ORF, and a 385-bp 3'-untranslated region. The ORF codes for a protein consisting of 358 amino acid residues and there existed one putative
20 transmembrane domain. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 43 kDa that was somewhat larger than the molecular weight
25 of 40,489 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa from which the secretory signal is considered to have been cleaved and a product of 43.5 kDa which is considered to have been subjected to some modification. Application of the
30 (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 23. When

expressed in COS7 cells, an expression product of about 44 kDa was observed in the supernatant fraction.

5 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein 39.9 kDa (SWISS-PROT Accession No. Q10005). Table 20 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein 39.9 kDa (CE).
10 Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 58.9% in the entire
15 region.

Determination of the whole base sequence of the cDNA insert of clone HP02419 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 253-bp

5'-untranslated region, a 681-bp ORF, and a 1120-bp 3'-untranslated region. The ORF codes for a protein consisting of 226 amino acid residues and there existed four putative transmembrane domains. Figure 32 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0108 (SWISS-PROT Accession No. Q15012). Table 21 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0108 (KI). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 43.9% in the entire region.

Table 21

```

HP      MKMVAPWTRFYSNSCCLCCHVRTGTILGVWYLIINAVVLLILLSALADPD---QY
      *****
5  KI  MVSMSEFKRNRSDRFYSTRCGCCHVRTGTIILGTWYMVVNLLMAILLTVETHPNMPEAV
      *****
HP  NFSSELGGDFEF-MDDANMCIAIAISLLMILICAMATYGAYKQRAAWIIPFFCYQIFDF
      *****
KI  NIQYEVIGNYYSSERMADNACVLFAVSVLMFIISMLVYGAISYQVGWLIPFFCYRLFDF
HP  ALNMLVAITVLIYPNSIQEYIRQLPPNFPYRDDVMSVNPTCLVLILLFISIIILTFKGYL
10 *****
      *. ****. *. *.*. *. ****. ....*.*.*.....*.*
KI  VLSCLVAISSLTYPRIKEYLDQL-PDFPYKDLLALDSSCLLFIVLVFFALFIIFKAYL
HP  ISCVWNCYRYINGRNSSDLVYVT-SNDTTVLLPPYDDATVNGAAKEPPPPYVSA
      *****
      *. ****. ....*.*.*.....*.*
KI  INCVWNCYKYYNNRVPEIAVYPAFEAPPQVVLPTY-EMAVKMPKEPPPPYLPA

```

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AAL73214) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02631> (SEQ ID Nos. 93, 103, and 113)

Determination of the whole base sequence of the cDNA insert of clone HP02631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 588-bp ORF, and a 750-bp 3'-untranslated region. Although the 49th amino acid residue is encoded by a stop codon, it is likely that this codon encodes selenocysteine from the molecular weight

of the translation product and the sequence comparison data with the *Caenorhabditis elegans* homologue. The ORF codes for a protein consisting of 195 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the intermediate region. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 58 kDa. In this case, the addition of a microsome led to the formation of a product of 56 kDa from which the secretory signal is considered to have been cleaved. Since both of these products are larger than the molecular weight of 22 kDa predicted from the ORF, it is likely that the protein interacts with another protein.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein C35C5.3 (EMBL Accession No. Z78417). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein C35C5.3 (CE). U at position 49 in the amino acid sequence of the protein of the present invention represents selenocysteine. Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.9% in the entire region other than the N-terminal region. Cystein was found in the sequence of the *C. elegans* protein at the position corresponding to position 49 encoded by the stop codon (selenocysteine) of the protein of the present invention.

untranslated region. The ORF codes for a protein consisting of 339 amino acid residues and there existed three putative transmembrane domains. Figure 34 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 38 kDa that was almost identical with the molecular weight of 38,274 kDa predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the rat hypertension-induced protein S-2 fragment (PIR Accession No. 539959). Table 23 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the rat hypertension-induced protein S-2 fragment (RN). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 74.3% in the entire region.

Table 23

HP MNWELLWLVLVLCALLLLLVQLLRFRLRADGDLTLWAEWQGRRPWEWELTDMVVVWVGASS

5 HP GIGEELAYQLSKLGVSLVLSARRVHELERVKRRCLENGNLKEKDILVPLDLTDTGSHEA
 ****.*****.***.

RN VKRRSLENGNLKEKDILVPLDLADTSSHDI

HP ATKAVLQEFGRIDILVNNGGMSQRSCLMDTSLDVYRKLIENLYLGTVSLTKCVLPHMIER

.**... ** *...*.***.***** **

10 RN ATKTVLQEFGRIDILVNNGGVAHASLVENTNMDIFKVLIEVNYLGTVSLTKCFLPHMMER

HP KQGKIIVTNSILGIISVPLSIGYCASKHALRGFFNGLRTELATYPGIIVSNICPGPVQSN

RN NQGKIIVMKS

15

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T84331) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10031> (SEQ ID Nos. 95, 105, and 115)

25 Determination of the whole base sequence of the cDNA insert of clone HP10031 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1464-bp ORF, and a 649-bp 3'-untranslated region. The ORF codes for a protein consisting of 487 amino acid residues and there existed eleven putative transmembrane domains. Figure 35 depicts the hydrophobicity/hydrophilicity profile, obtained

30

by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELK07H8 (GenBank Accession No. AF047659). Table 24 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CELK07H8 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.2% in the entire region.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA334000) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5

<HP10530> (SEQ ID Nos. 96, 106, and 116)

Determination of the whole base sequence of the cDNA insert of clone HP10530 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure
10 consisting of a 80-bp 5'-untranslated region, a 1182-bp ORF, and a 95-bp 3'-untranslated region. The ORF codes for a protein consisting of 393 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 36 depicts the hydrophobicity/hydrophilicity profile,
15 obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 46 kDa that was somewhat larger than the molecular weight of 44,912 predicted from the ORF. In this case, the addition of a microsome led to the formation
20 of a product of 45.5 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from lysine at position 23. When expressed in
25 COS7 cells, an expression product of about 43 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the
30 protein was similar to the Arabidopsis thaliana hypothetical protein IG002N01 (GenBank Accession No. AF007269). Table 25 shows the comparison between amino acid sequences of the

human protein of the present invention (HP) and the A.
thaliana hypothetical protein IG002N01 (AT). Therein, the
marks of -, *, and . represent a gap, an amino acid residue
identical with that of the protein of the present invention,
5 and an amino acid residue similar to that of the protein of
the present invention, respectively. The both proteins
shared a homology of 27.0% in the N-terminal region of 355
amino acid residues.

Table 25

HP	MRTLFLNLLWL
5	AT MELTSFQKSPSSNDVVSFVSVSLVRNSMARRRRSSAAESLKRNDGYESLCQVVQQDSDRR HP ALACSPVHTTLSKSDAKKAASKTLEKSQFSDKPVQDRGLVVDLKAESVVLHRSYCSA*.*.*.*.....
10	AT LITIFVIFFIVIPAVSIAVYKVKFADRVIQTESSIRQKGIVKTDINFQEILTEHSK--AS HP KARDRH FAGDVLGYVTPWN SHGYDVT KVFSGKFTQISPVWLQ-LKRRGREMFVETGLHDV*.*.*.*.....
15	AT ENSTRHYDYPVLAYITP--CQSGSL--VLEGR-HNADKGWIELRSRGNALSASKGLPKL HP DQGWMR A VRKHAKGLHIVPRL LFEDWTDYDDFRNVLDSEDEIEELSKTVVQVAKNQHFDDGF*.*.*.*.....
20	AT ---YNSCIFHALKRMNFFTLELVNFNTYLVIMFALNS-REMEYNGIVLESWSWAAAYGVL HP VVEVWNQLLSQKRVGLIHMLTHLAEALHQARLLALLVIPPAITPGTDQLGMFTHKEFEQL*.*.*.*.....
25	AT HDPDLRKMALKFVKQLGDALHSTSSPRNNQOHMQFMVVGPPRSEKLQMYDFGPEDLQFL HP APVLDGFSLMTYDYSTAHPGP NAPLSWVRACVQ-VLDPKSK----WRSKILLGLNIFYGM*.*.*.*.....
30	AT KDSVDGFSLMTYDFSNPQNPGNAPVKWIDLTLKLLGSSNNIDSNIAKRVLLGINIFYGN HP DYATSKDAREPVVGARYIQTLDHRPRMVWDSQASEHFFEYKKSRSGRHVVFYPTLKSLQ*.*.*.*.....
35	AT DFVISGGGGGAIITGRDYLALLQKHKPTFRWDKESGEHLFMYRDDKNIKHAVFYPTLMSIL HP VRLELARELGVGVSIELWGQGLDYFYDLL*.*.*.*.....
40	AT LRLENARLWIGIGISIWEIGQDKGHFGKYAEASLEASSIFSGHTFDMQFRTNPQRLSRNGS

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA302913) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the

protein of the present invention.

<HP10541> (SEQ ID Nos. 97, 107, and 117)

Determination of the whole base sequence of the cDNA
insert of clone HP10541 obtained from cDNA library of human
stomach cancer revealed the structure consisting of a 7-bp
5'-untranslated region, a 591-bp ORF, and a 113-bp 3'-
untranslated region. The ORF codes for a protein consisting
of 196 amino acid residues and there existed a putative
secretory signal at the N-terminus. Figure 37 depicts the
hydrophobicity/hydrophilicity profile, obtained by the Kyte-
Doolittle method, of the present protein. In vitro
translation resulted in formation of a translation product
of 23 kDa that was somewhat larger than the molecular weight
of 21,553 predicted from the ORF. In this case, the addition
of a microsome led to the formation of a product of 20 kDa
from which the secretory signal is considered to have been
cleaved and a product of 23 kDa which is considered to have
a sugar chain being attached. Application of the (-3,-1)
rule, a method for predicting the cleavage site of the
secretory signal sequence, allows to expect that the mature
protein starts from glycine at position 41. In addition,
there exists in the amino acid sequence of this protein one
site at which N-glycosylation may occur (Asn-Leu-Thr at
position 185).

The search of the protein data base using the amino
acid sequence of the present protein revealed that the
protein was similar to the human zymogen membrane protein
(GenBank Accession No. AF056492). Table 26 shows the
comparison between amino acid sequences of the human protein
of the present invention (HP) and the human zymogen membrane
protein (ZM). Therein, the marks of -, *, and . represent a

insert of clone HP10550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 241-bp 5'-untranslated region, a 324-bp ORF, and a 86-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 38 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA348310) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10590> (SEQ ID Nos. 99, 109, and 119)

Determination of the whole base sequence of the cDNA insert of clone HP10590 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 77-bp 5'-untranslated region, a 1053-bp ORF, and a 180-bp 3'-untranslated region. The ORF codes for a protein consisting of 350 amino acid residues and there existed one putative transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,285 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of

43 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Asn-Ser at position 144 and Asn-Leu-Thr at position 328).

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA461346) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10591> (SEQ ID Nos. 100, 110, and 120)

Determination of the whole base sequence of the cDNA insert of clone HP10591 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 232-bp 5'-untranslated region, a 324-bp ORF, and a 844-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 40 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,328 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H09424) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

of the present invention.

<HP01462> (SEQ ID Nos. 121, 131, and 141)

Determination of the whole base sequence of the cDNA
5 insert of clone HP01462 obtained from cDNA library of human
fibrosarcoma cell line HT-1080 revealed the structure
consisting of a 121-bp 5'-untranslated region, a 1452-bp ORF,
and a 477-bp 3'-untranslated region. The ORF codes for a
protein consisting of 483 amino acid residues and there
10 existed a putative secretory signal at the N-terminus.
Figure 41 depicts the hydrophobicity/hydrophilicity profile,
obtained by the Kyte-Doolittle method, of the present
protein. In vitro translation resulted in formation of a
translation product of 72 kDa that was larger than the
15 molecular weight of 55,838 predicted from the ORF.
Application of the (-3,-1) rule, a method for predicting the
cleavage site of the secretory signal sequence, allows to
expect that the mature protein starts from lysine at
position 21.

20 The search of the protein data base using the amino
acid sequence of the present protein revealed that the
protein was similar to the *Caenorhabditis elegans*
hypothetical protein ZK1058.4 (EMBL Accession No. Z35604).
Table 27 shows the comparison between amino acid sequences
25 of the human protein of the present invention (HP) and the *C.*
elegans hypothetical protein ZK1058.4 (CE). Therein, the
marks of -, *, and . represent a gap, an amino acid residue
identical with that of the protein of the present invention,
and an amino acid residue similar to that of the protein of
30 the present invention, respectively. The both proteins
shared a homology of 35.6% in the entire region.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA307793) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5

<HP02485> (SEQ ID Nos. 122, 132, and 142)

Determination of the whole base sequence of the cDNA insert of clone HP02485 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 69-bp
10 5'-untranslated region, a 1005-bp ORF, and a 1672-bp 3'-untranslated region. The ORF codes for a protein consisting of 334 amino acid residues and there existed one putative transmembrane domain. Figure 42 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro
15 translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 38,171 predicted from the ORF. When expressed in COS7 cells, an expression product of about 23 kDa was
20 observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein W01A11.2 (GenBank Accession No. U64852).
25 Table 28 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein W01A11.2 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of
30 the present invention, respectively. The both proteins shared a homology of 45.5% in the entire region.

Determination of the whole base sequence of the cDNA

insert of clone HP02798 obtained from cDNA library of human
fibrosarcoma cell line HT-1080 revealed the structure
consisting of a 31-bp 5'-untranslated region, a 804-bp ORF,
and a 301-bp 3'-untranslated region. The ORF codes for a
5 protein consisting of 267 amino acid residues and there
existed four putative transmembrane domains. Figure 43
depicts the hydrophobicity/hydrophilicity profile, obtained
by the Kyte-Doolittle method, of the present protein. In
vitro translation resulted in formation of a translation
10 product of 29 kDa that was almost identical with the
molecular weight of 30,778 predicted from the ORF. When
expressed in COS7 cells, an expression product of about 26
kDa was observed in the membrane fraction.

The search of the protein data base using the amino
15 acid sequence of the present protein revealed that the
protein was similar to the human DHHC-containing cysteine-
rich protein (GenBank Accession No. U90653). Table 29 shows
the comparison between amino acid sequences of the human
protein of the present invention (HP) and the human DHHC-
20 containing cysteine-rich protein (DH). Therein, the marks of
-, *, and . represent a gap, an amino acid residue identical
with that of the protein of the present invention, and an
amino acid residue similar to that of the protein of the
present invention, respectively. The both proteins shared a
25 homology of 35.0% in the intermediate region of 100 amino
acid residues. The positions of seven cysteines were
conserved between the two proteins. The protein of the
present invention also had the DHHC (Asp-His-His-Cys)
sequence.

Determination of the whole base sequence of the cDNA insert of clone HP10041 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 12-bp 5'-untranslated region, a 321-bp ORF, and a 286-bp 3'-untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 44 depicts

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the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 12,060 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein K10B2.4 (GenBank Accession No. U28730). Table 30 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein K10B2.4 (CE). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 62.1% in the entire region.

Table 30

HP	MSTNNMSDPRRPNKVLRYP---PPSECNPALDDPTPDYMNLLGMIFSMCGLMIRKRWCA
	*****.....** *.....*
CE	MQQNGDPRRTNRIVRYKPLDSTANQQQAISEDPLPEYMNVLGMIFSMCGLMIRKRWCS
HP	WVAVYCSFISFANSRSEDTRQMMSSFMLSISAVVMSYLNQNPQPMTPPW
	. ** *****.*.*.*.....***** *.***
CE	WLALVCSCISFANTRTSDDAKQIVSSFMLSVSASVMSYLNQNPPIPPWVTLQ

Furthermore, the search of the GenBank using the base

sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H20098) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10246> (SEQ ID Nos. 125, 135, and 145)

Determination of the whole base sequence of the cDNA insert of clone HP10246 obtained from cDNA library of human epidermoid carcinoma cell line KB revealed the structure consisting of a 110-bp 5'-untranslated region, a 675-bp ORF, and a 79-bp 3'-untranslated region. The ORF codes for a protein consisting of 224 amino acid residues and there existed five putative transmembrane domains. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was somewhat smaller than the molecular weight of 25,244 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human putative seven transmembrane domain protein (GenBank Accession No. Y18007). Table 31 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human putative seven transmembrane domain protein (TM). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

of the protein of the present invention, respectively. The both proteins shared a homology of 93.3% in the entire region.

5

Table 31

```

HP MTLFHFNCFCALAYFPYFITYKCSGLSEYNFAFWKCVQAGVTYLFVQLCKMLFLATFFPTW
*****
TM MTLFHFNCFCALAYFPYFITYKCTDLSEYNFAFWKCVQAGVTYLFVQLCKMLFLATFFPTW
HP EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
*****
TM EGGIYDFIGEFMKASVDVADLIGLNLVMSRNAGKGEYKIMVAALGWATAELIMSRCIPLW
HP VGARGIEFDWKYIQMSIDSNISLVHYIVASAQVWMITRYDLYHTFRPAVLLLMFLSVYKA
*****
15 TM VGARGIEFDWKYIQMSIDSNISLGPYIVASAQVWMITRYDLYHTFRPAVLLLMFLRVYKA
HP FVMETFVHLCSLGSWAALLARAVVTGLLSTLALYVAVNVVHS
*****
TM FVMETFVHLCSLGSWAVLMAGVVVKGLLVIRNLAMYVAVNVVHS

```

20

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA453931) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25

<HP10392> (SEQ ID Nos. 126, 136, and 146)

30

Determination of the whole base sequence of the cDNA insert of clone HP10392 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure

consisting of a 24-bp 5'-untranslated region, a 777-bp ORF, and a 726-bp 3'-untranslated region. The ORF codes for a protein consisting of 258 amino acid residues and there existed a putative secretory signal at the N-terminus.

- 5 Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was somewhat larger than the molecular weight of 29,623 predicted from the ORF.
- 10 Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 49.

- 15 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H15999) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein
- 20 of the present invention. In addition, partial identity with the hypothetical protein KIAA0384 (Accession No. AB002382) was observed, although the hypothetical protein had a different ORF.

- 25 <HP10489> (SEQ ID Nos. 127, 137, and 147)

- Determination of the whole base sequence of the cDNA insert of clone HP10489 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 137-bp 5'-untranslated region, a 333-bp ORF, and a 189-bp 3'-untranslated region. The ORF codes for a protein consisting of 110 amino acid residues and there existed two putative transmembrane domains. Figure 47 depicts the
- 30

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 12,010 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA262162) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10519> (SEQ ID Nos. 128, 138, and 148)

Determination of the whole base sequence of the cDNA insert of clone HP10519 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 67-bp 5'-untranslated region, a 276-bp ORF, and a 367-bp 3'-untranslated region. The ORF codes for a protein consisting of 91 amino acid residues and there existed one putative transmembrane domain. Figure 48 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,275 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W16639) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

of the present invention.

<HP10531> (SEQ ID Nos. 129, 139, and 149)

Determination of the whole base sequence of the cDNA
5 insert of clone HP10531 obtained from cDNA library of human
osteosarcoma cell line Saos-2 revealed the structure
consisting of a 55-bp 5'-untranslated region, a 1035-bp ORF,
and a 1092-bp 3'-untranslated region. The ORF codes for a
protein consisting of 344 amino acid residues and there
10 existed five putative transmembrane domains. Figure 49
depicts the hydrophobicity/hydrophilicity profile, obtained
by the Kyte-Doolittle method, of the present protein. In
vitro translation resulted in formation of a translation
product of high molecular weight.

15 Furthermore, the search of the GenBank using the base
sequences of the present cDNA has revealed the registration
of sequences that shared a homology of 90% or more (for
example, Accession No. R50695) in ESTs, but, since they are
partial sequences, it can not be judged whether or not any
20 of these sequences codes for the same protein as the protein
of the present invention.

<HP10574> (SEQ ID Nos. 130, 140, and 150)

Determination of the whole base sequence of the cDNA
25 insert of clone HP10574 obtained from cDNA library of human
stomach cancer revealed the structure consisting of a 210-bp
5'-untranslated region, a 1287-bp ORF, and a 1276-bp 3'-
untranslated region. The ORF codes for a protein consisting
of 428 amino acid residues and there existed a putative
30 secretory signal at the N-terminus and one putative
transmembrane domain in the intermediate region. Figure 50
depicts the hydrophobicity/hydrophilicity profile, obtained

by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from serine at position 36.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Drosophila melanogaster* GOLIATH protein (SWISS-PROT Accession No. Q06003). Table 32 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *D. melanogaster* GOLIATH protein (DM). Therein, the marks of -, *, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The intermediate region of 169 amino acids of the protein of the present invention shared a homology of 41.4% with the N-terminal region of the *D. melanogaster* GOLIATH protein.

The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. All of the proteins of the present invention are secreted or exist in the cell membrane, so that they are considered to be proteins controlling the proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents which act to control the proliferation and/or the differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for large-scale expression of these proteins. Cells into which these genes are introduced to express these proteins, can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or

primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished

through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s). Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more

preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides

capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the

5 table 33 below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R.

Table 33

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp) [‡]	Hybridization Temperature and Buffer [†]	Wash Temperature and Buffer [†]
A	DNA : DNA	≥50	65°C; 1×SSC -or- 42°C; 1×SSC, 50% formamide	65°C; 0.3×SSC
B	DNA : DNA	<50	T _B *; 1×SSC	T _B *; 1×SSC
C	DNA : RNA	≥50	67°C; 1×SSC -or- 45°C; 1×SSC, 50% formamide	67°C; 0.3×SSC
D	DNA : RNA	<50	T _D *; 1×SSC	T _D *; 1×SSC
E	RNA : RNA	≥50	70°C; 1×SSC -or- 50°C; 1×SSC, 50% formamide	70°C; 0.3×SSC
F	RNA : RNA	<50	T _F *; 1×SSC	T _F *; 1×SSC
G	DNA : DNA	≥50	65°C; 4×SSC -or- 42°C; 4×SSC, 50% formamide	65°C; 1×SSC
H	DNA : DNA	<50	T _H *; 4×SSC	T _H *; 4×SSC
I	DNA : RNA	≥50	67°C; 4×SSC -or- 45°C; 4×SSC, 50% formamide	67°C; 1×SSC
J	DNA : RNA	<50	T _J *; 4×SSC	T _J *; 4×SSC
K	RNA : RNA	≥50	70°C; 4×SSC -or- 50°C; 4×SSC, 50% formamide	67°C; 1×SSC
L	RNA : RNA	<50	T _L *; 2×SSC	T _L *; 2×SSC
M	DNA : DNA	≥50	50°C; 4×SSC -or- 40°C; 6×SSC, 50% formamide	50°C; 2×SSC
N	DNA : DNA	<50	T _N *; 6×SSC	T _N *; 6×SSC
O	DNA : RNA	≥50	55°C; 4×SSC -or- 42°C; 6×SSC, 50% formamide	55°C; 2×SSC
P	DNA : RNA	<50	T _P *; 6×SSC	T _P *; 6×SSC
Q	RNA : RNA	≥50	60°C; 4×SSC -or- 45°C; 6×SSC, 50% formamide	60°C; 2×SSC
R	RNA : RNA	<50	T _R *; 4×SSC	T _R *; 4×SSC

‡: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

†: SSPE (1×SSPE is 0.15M NaCl, 10mM NaH₂PO₄, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

*T_B - T_R: The hybridization temperature for hybrids anticipated to be less than

50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, $T_m(^{\circ}\text{C}) = 2(\text{\# of A + T bases}) + 4(\text{\# of G + C bases})$. For hybrids between 18 and 49 base pairs in length, $T_m(^{\circ}\text{C}) = 81.5 + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\%(\text{G+C}) \cdot (600/\text{N}))$, where N is the number of bases in the hybrid, and $[\text{Na}^+]$ is the concentration of sodium ions in the hybridization buffer ($[\text{Na}^+]$ for $1\times\text{SSC}=0.165\text{M}$).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

CLAIMS

1. A protein comprising any one of an amino acid sequence selected from the group consisting of SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

2. An isolated DNA coding for the protein according to Claim 1.

3. An isolated cDNA comprising any one of a base sequence selected from the group consisting of SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140.

4. The cDNA according to Claim 3 consisting of any one of a base sequence selected from the group consisting of SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150.

5. An expression vector that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 by in vitro translation or in eucaryotic cells.

6. A transformed eucaryotic cell that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 and of producing the protein according to Claim 1.

PCT

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/JP99/03929 (22) International Filing Date: 22 July 1999 (22.07.99) (30) Priority Data: 10/208820 24 July 1998 (24.07.98) JP 10/224105 7 August 1998 (07.08.98) JP 10/238116 25 August 1998 (25.08.98) JP 10/254736 9 September 1998 (09.09.98) JP 10/275505 29 September 1998 (29.09.98) JP (71) Applicants (for all designated States except US): SAGAMI CHEMICAL RESEARCH CENTER [JP/JP]; 4-1, Nishi-Ohnuma 4-chome, Sagamihara-shi, Kanagawa 229-0012 (JP). PROTEGENE INC. [JP/JP]; 2-20-3, Naka-cho, Meguro-ku, Tokyo 153-0065 (JP). (72) Inventors; and (75) Inventors/Applicants (for US only): KATO, Seishi [JP/JP]; 3-46-50, Wakamatsu, Sagami-hara-shi, Kanagawa 229-0014 (JP). KIMURA, Tomoko [JP/JP]; 302, 4-1-28, Nishikutu, Tama-ku, Kawasaki-shi, Kanagawa 214-0037 (JP).		(74) Agents: AOYAMA, Tamotsu et al.; Aoyama & Partners, IMP Building, 3-7, Shiromi 1-chome, Chuo-ku, Osaka-shi, Osaka 540-0001 (JP). (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims</i> <i>and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 4 May 2000 (04.05.00)
(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS (57) Abstract <p>The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.</p>		

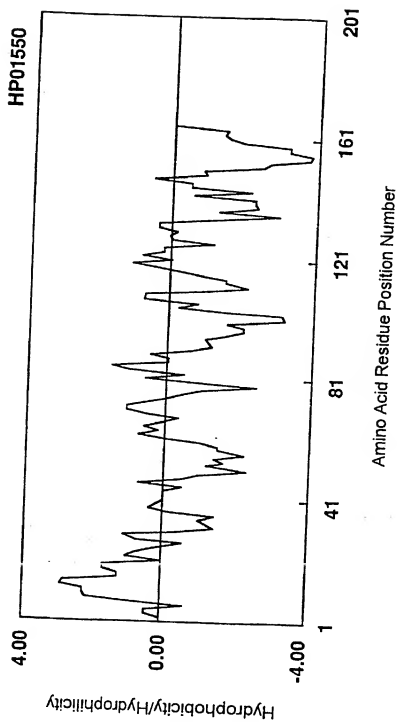


Fig. 1

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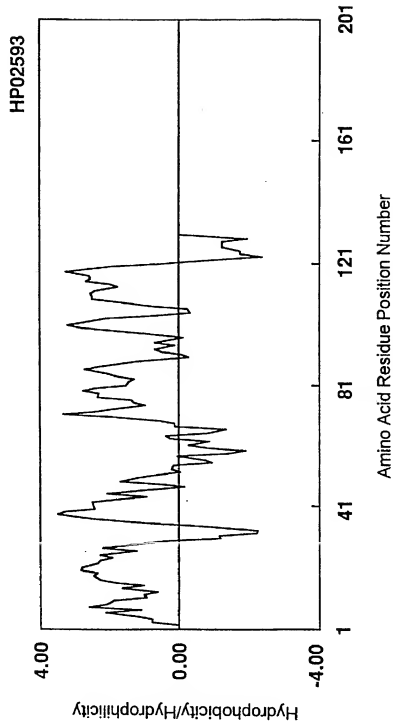


Fig. 2

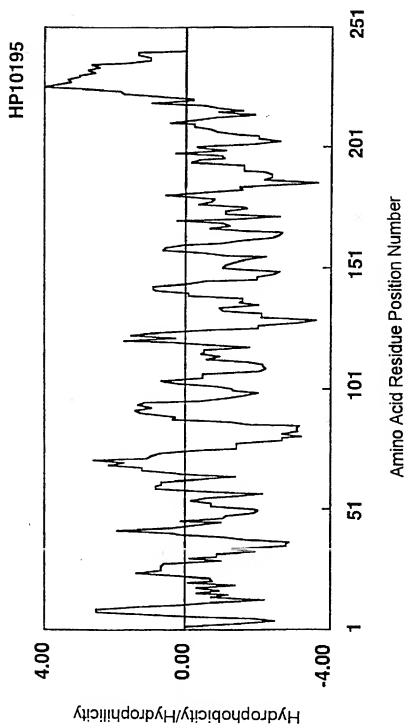


Fig. 3

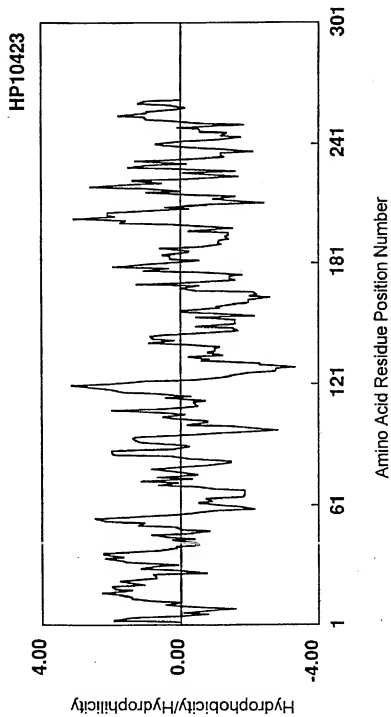


Fig. 4

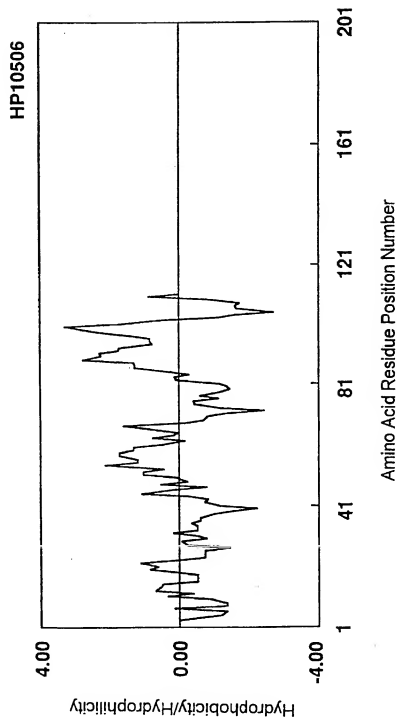


Fig. 5

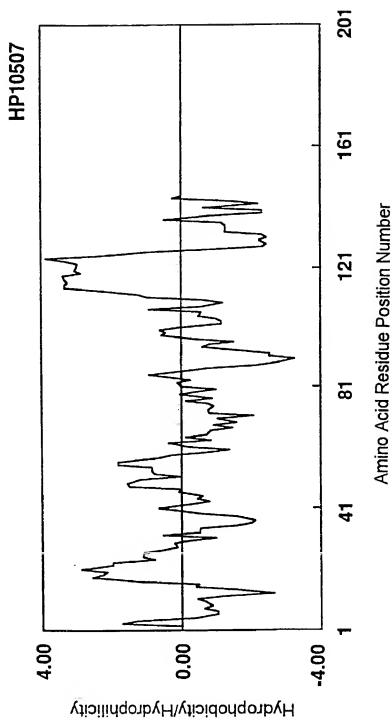


Fig. 6

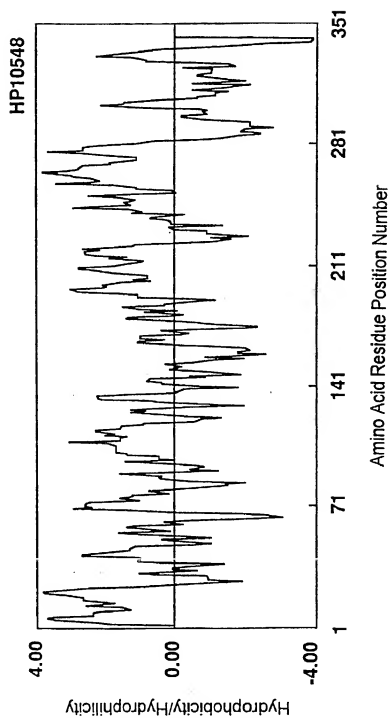


Fig. 7

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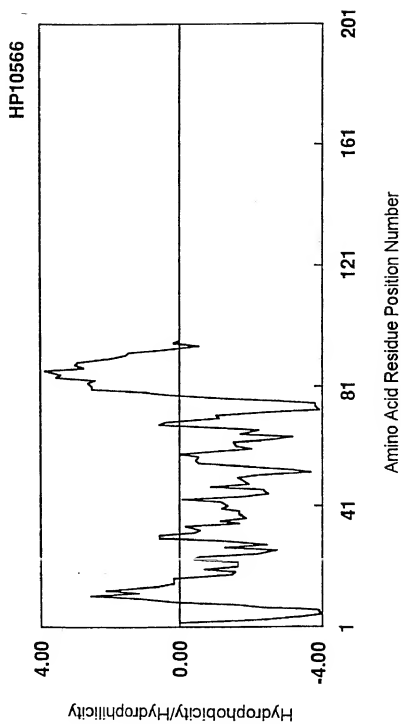


Fig. 8

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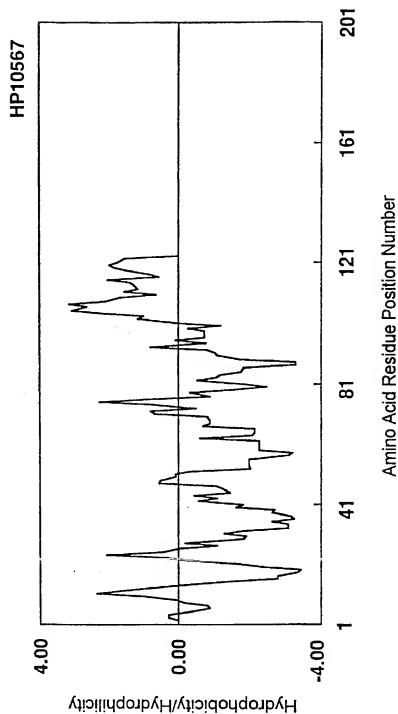


Fig. 9

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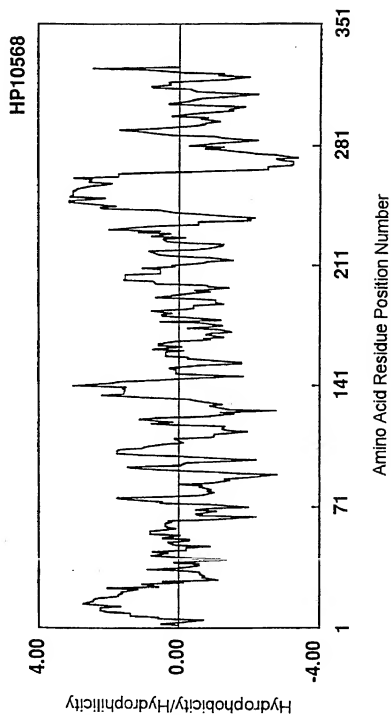


Fig. 10

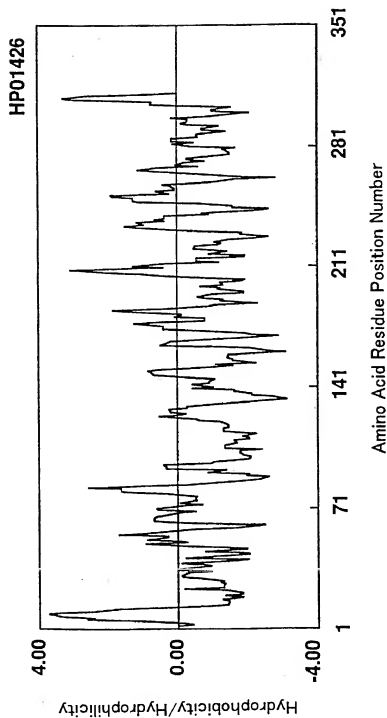


Fig. 11

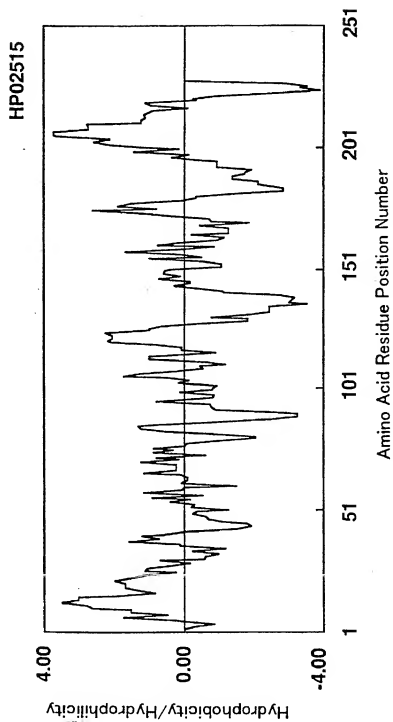


Fig.12

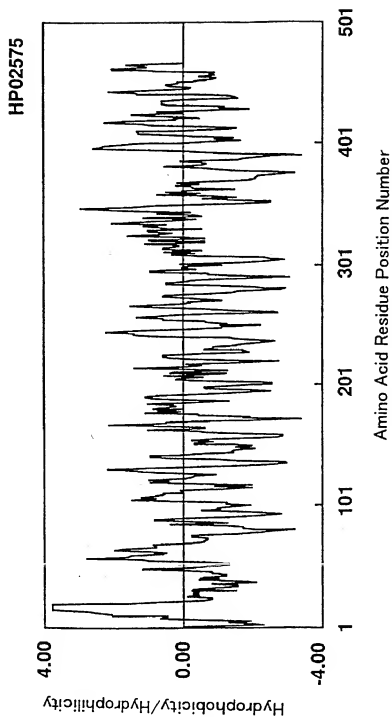


Fig. 13

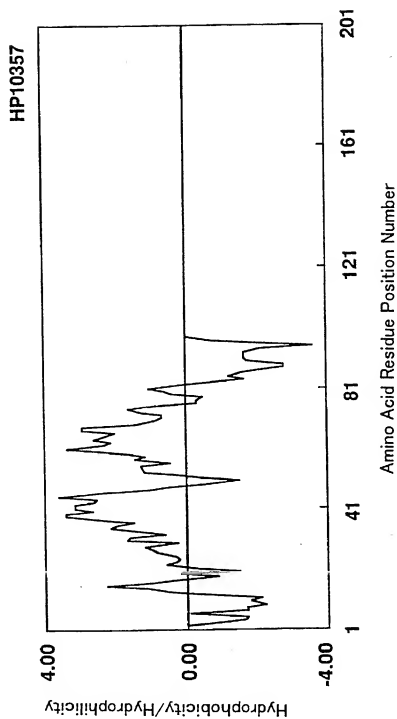


Fig. 14

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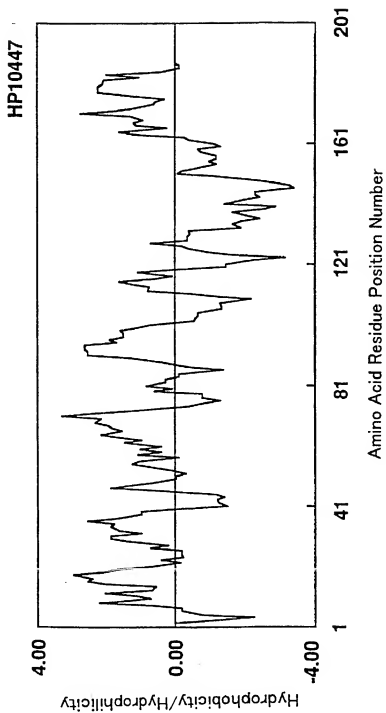


Fig. 15

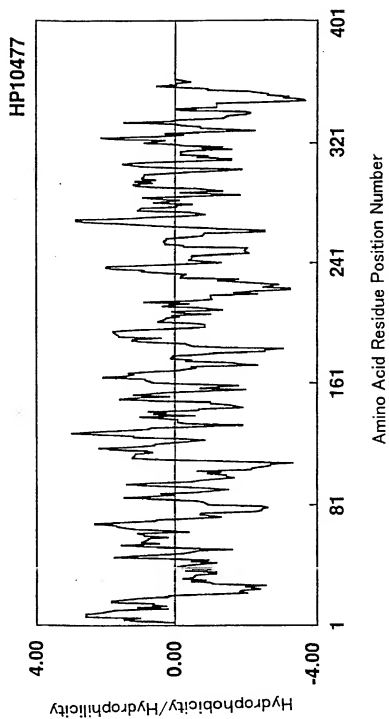


Fig. 16

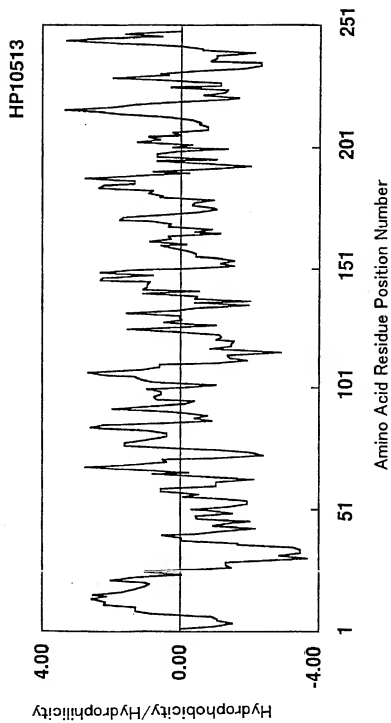


Fig.17

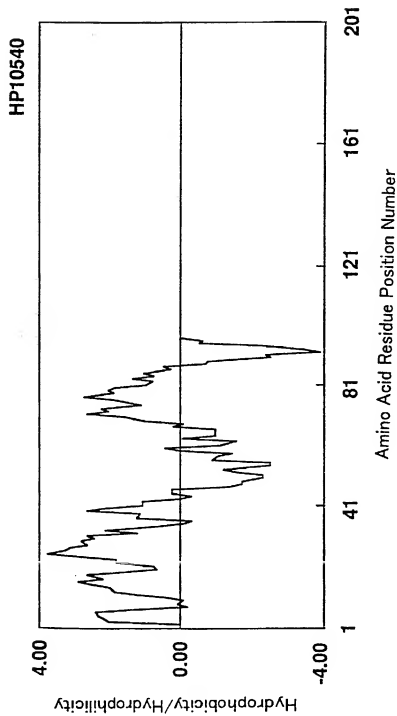


Fig. 18

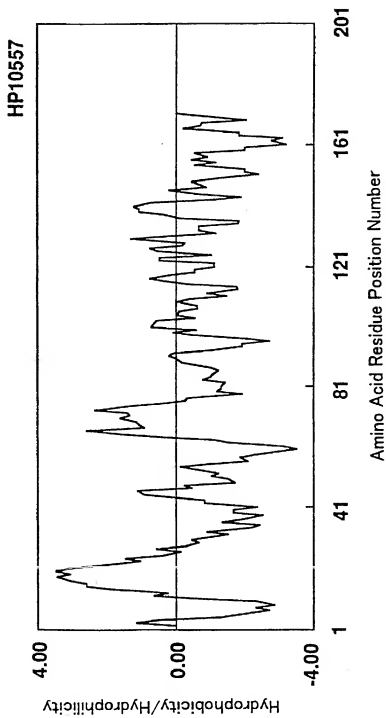


Fig. 19

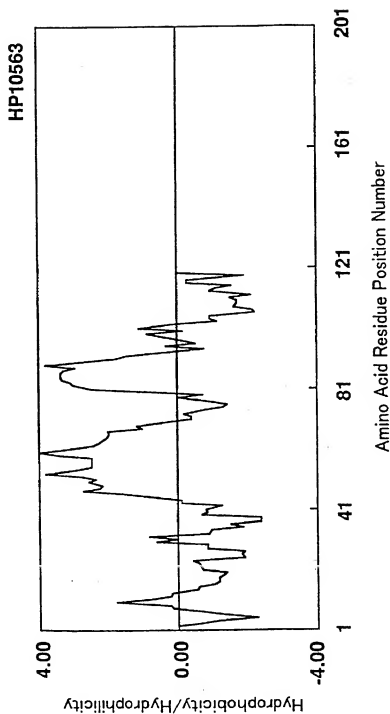


Fig. 20

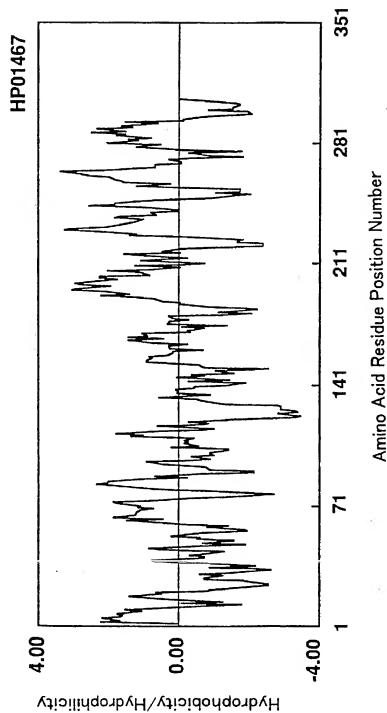


Fig. 21

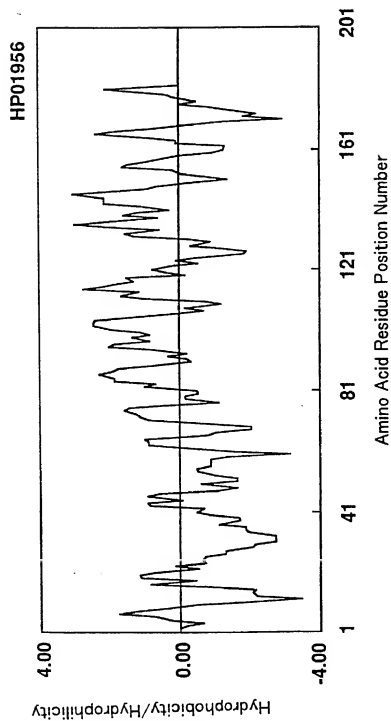


Fig.22

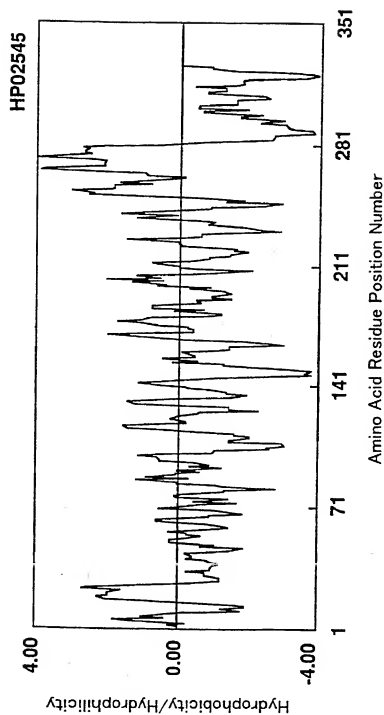


Fig. 23

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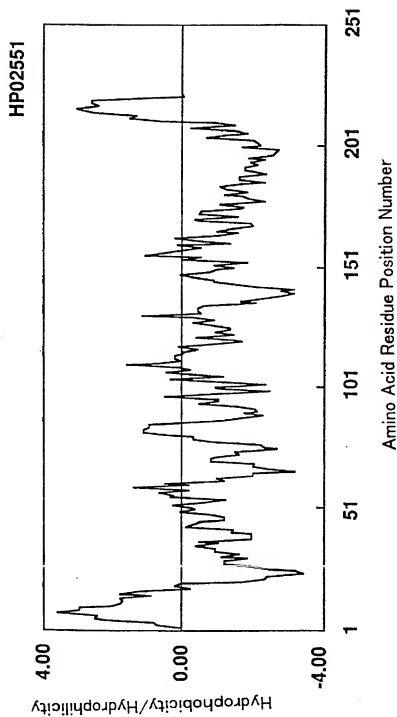


Fig. 24

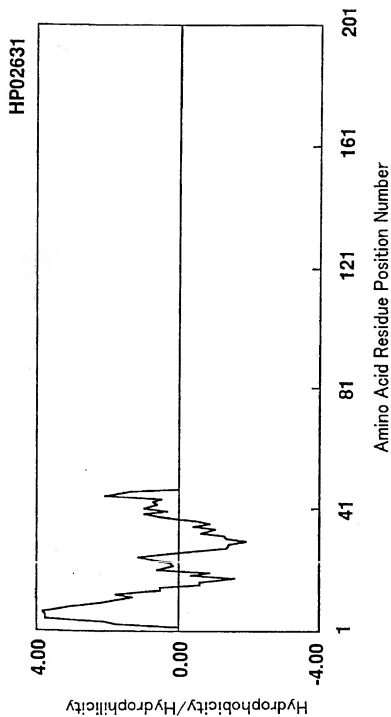


Fig. 25

09743307 09743307 09/743247

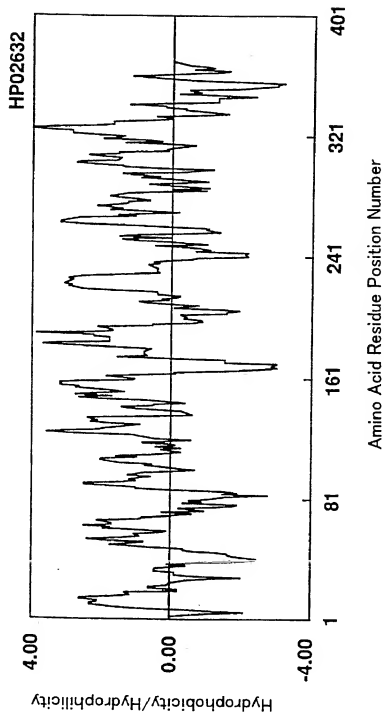


Fig. 26

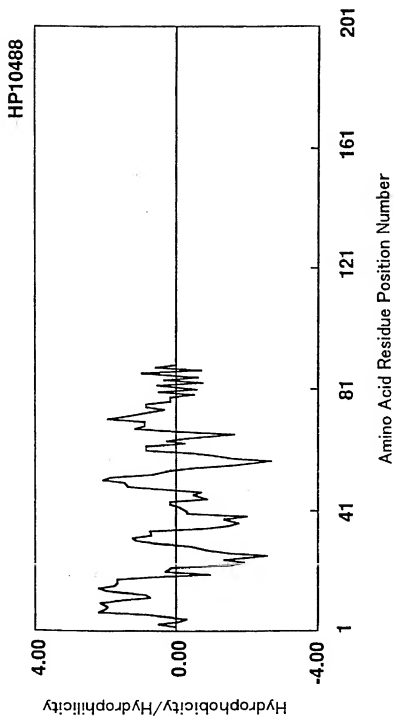


Fig.27

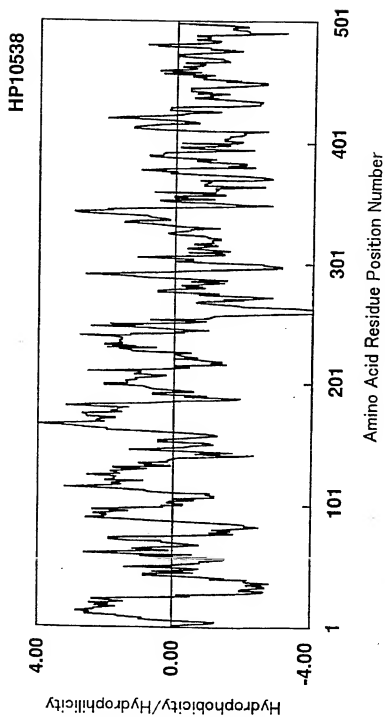


Fig. 28

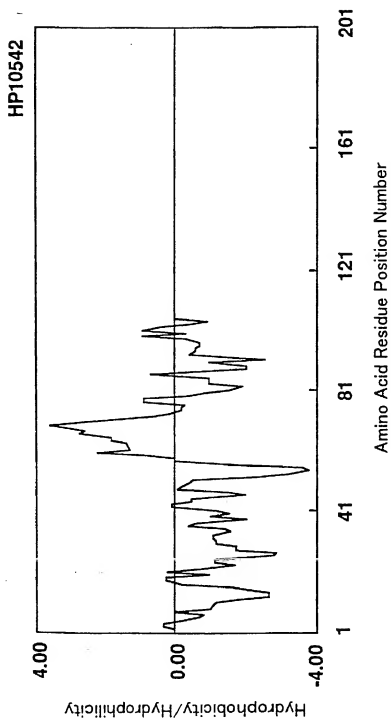


Fig. 29

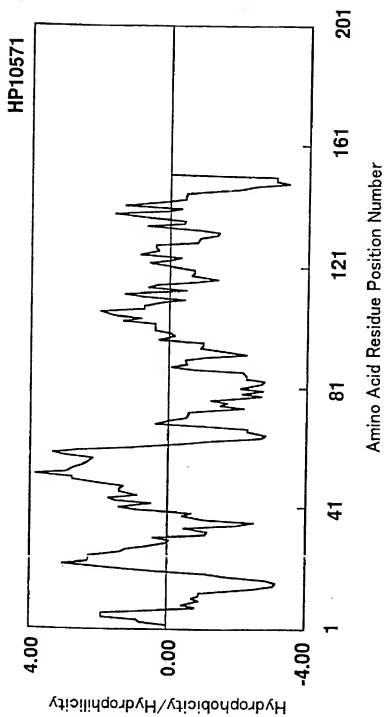


Fig. 30

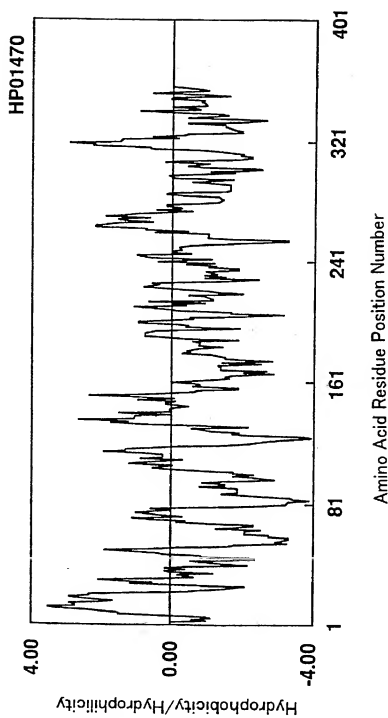


Fig. 31

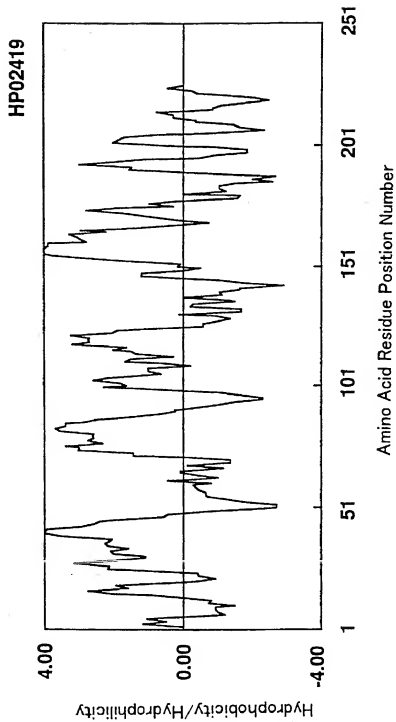


Fig.32

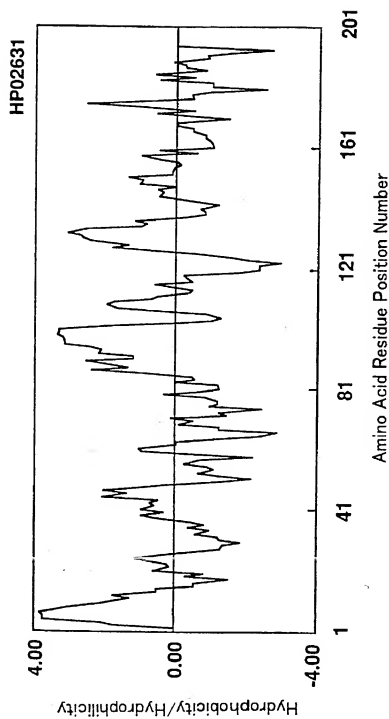


Fig. 33

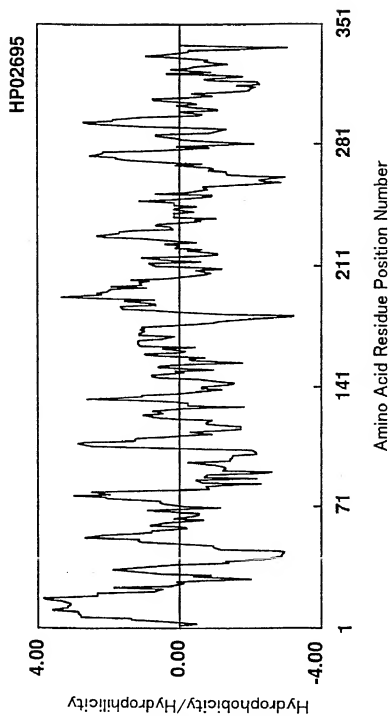


Fig. 34

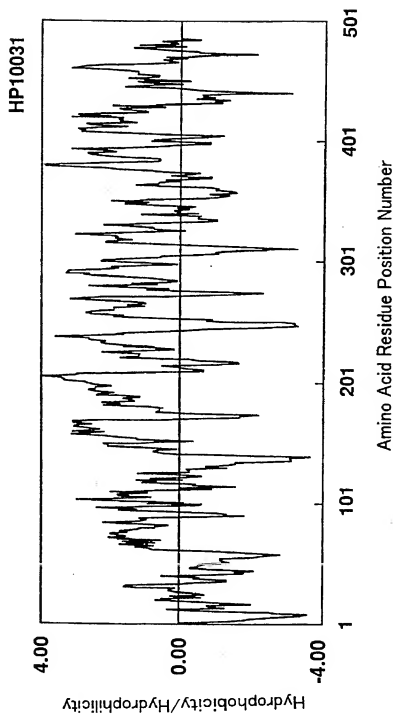


Fig. 35

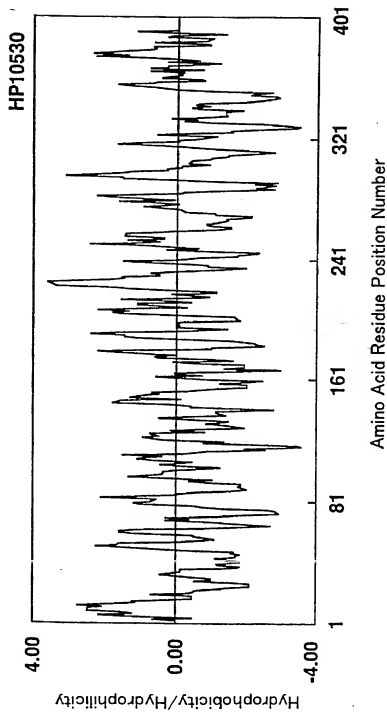


Fig. 36

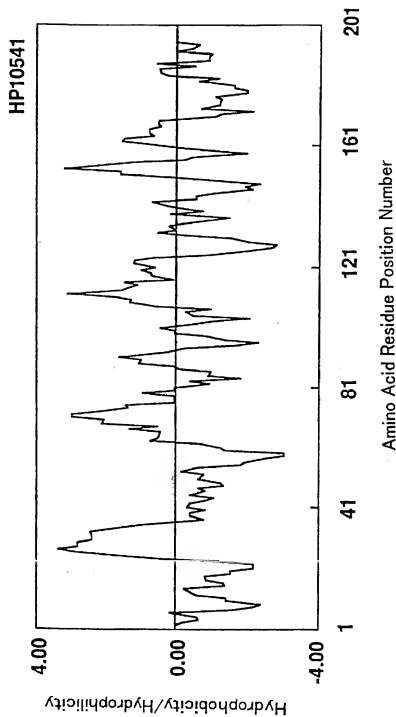


Fig.37

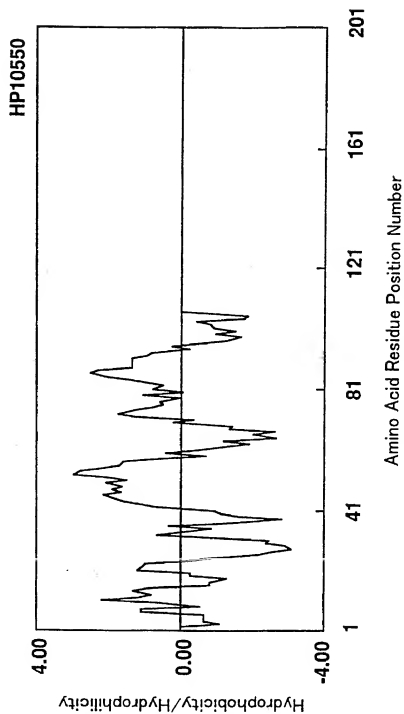


Fig. 38

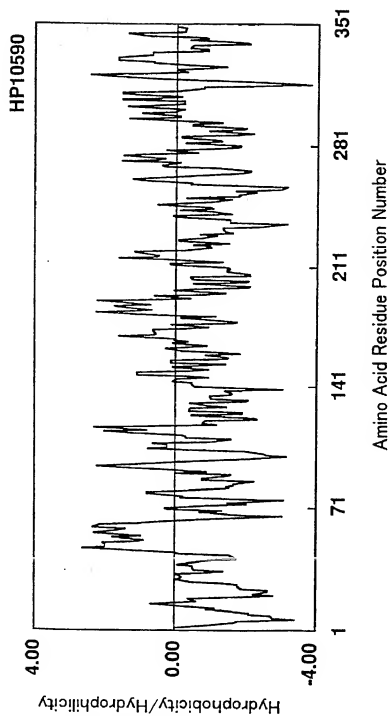


Fig. 39

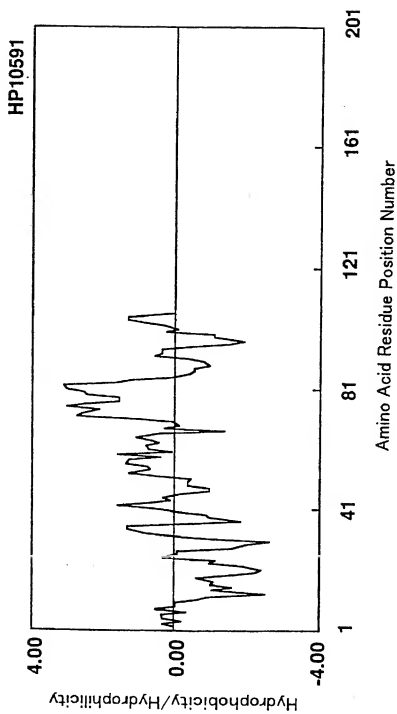


Fig. 40

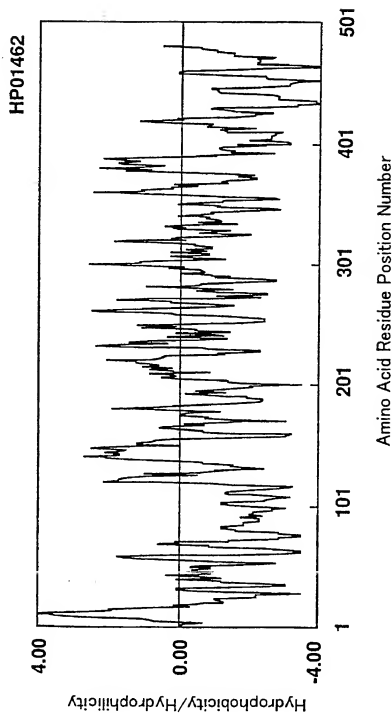


Fig. 41

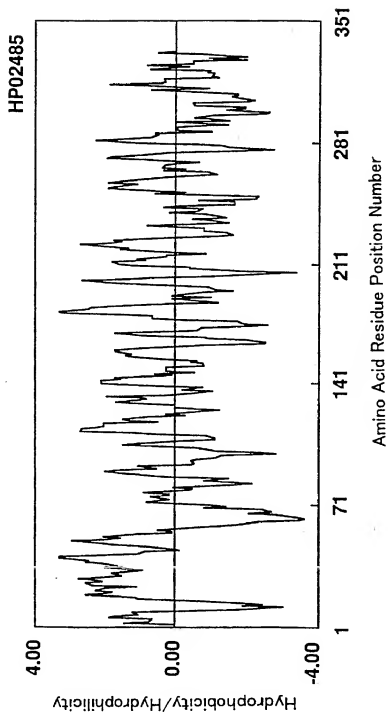


Fig.42

09/743247

09743247.062601

09/743247

WO 00/05367

PCT/JP99/03929

43/50

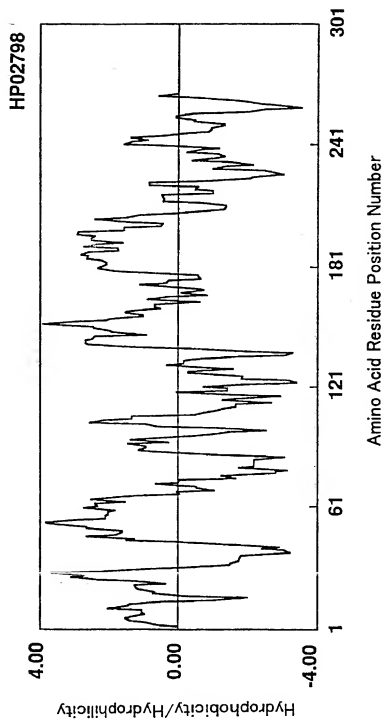


Fig. 43

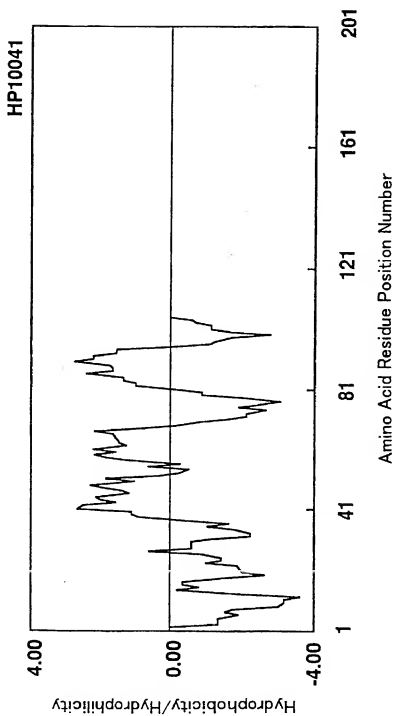


Fig. 44

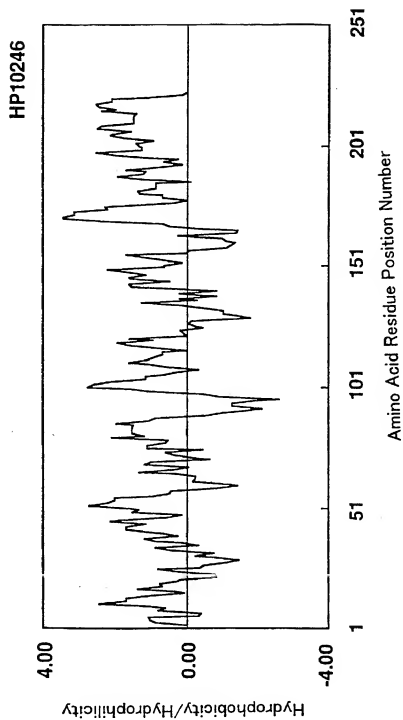


Fig. 45

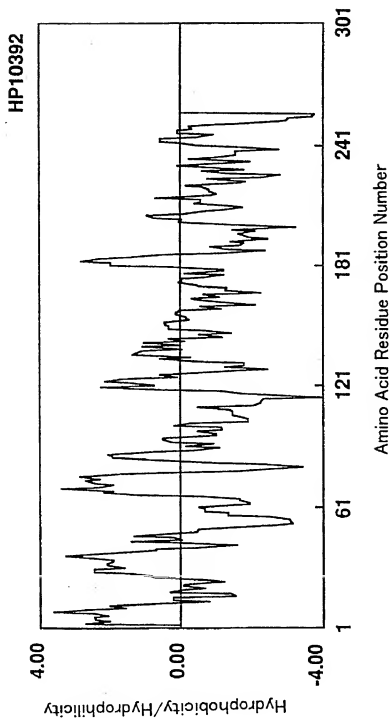


Fig. 46

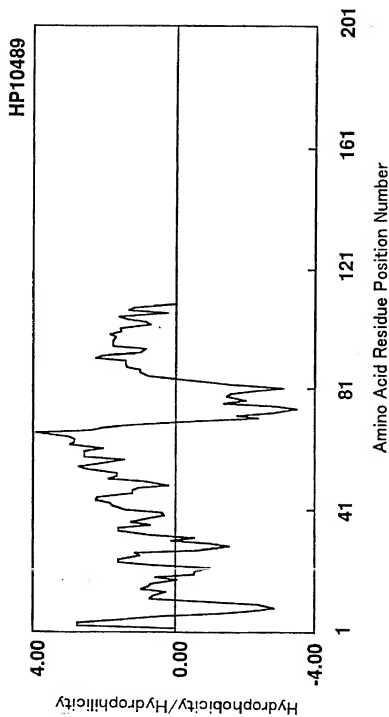


Fig.47

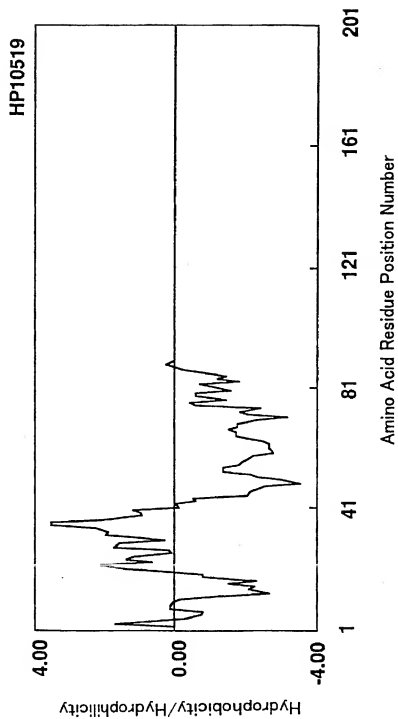


Fig. 48

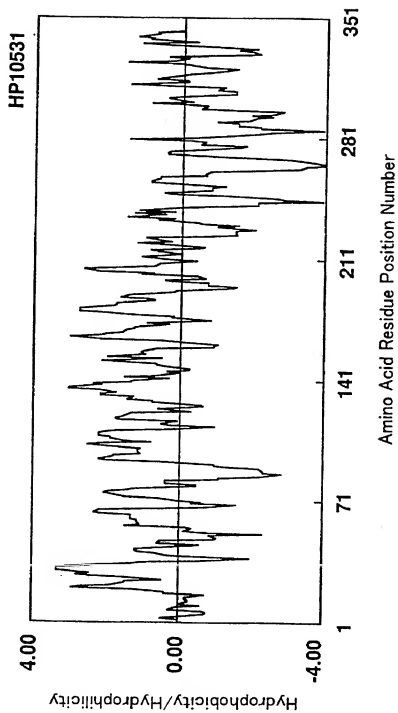


Fig. 49

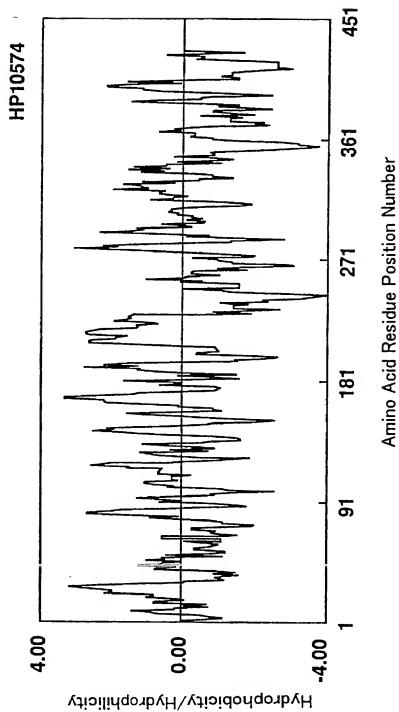


Fig. 50

Atty Docket No.: GIN-6718CP5US**DECLARATION, PETITION AND POWER OF ATTORNEY
FOR PATENT APPLICATION**

(Check one):

- ☐ Declaration Submitted with Initial Filing
☒ Declaration Submitted after Initial Filing

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS
AND DNAs ENCODING THESE PROTEINS**

the specification of which (check one):

- ☐ is attached hereto.
OR
☒ was filed on 5 January 2001 as U.S. National Application Serial No. 09/743,247
(U.S. National Filing of PCT/JP99/03929 filed on 22 July 1999).
- ☐ and was amended by PCT Article 19 Amendment on _____
(if applicable),
- ☐ and was amended by PCT Article 34 Amendment on _____
(if applicable).

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby state that I have reviewed and understood the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

PRIORITY CLAIM

(Check one):

- ☐ no such applications have been filed.
- ☒ such applications have been filed as follows

1) FOREIGN PRIORITY CLAIM: I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate or §365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (dd/mm/yyyy)	Priority Not Claimed	Certified Copy Attached	
				Yes	No
10/275505	JP	29/09/1998	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
10/254736	JP	09/09/1998	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
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10/224105	JP	07/08/1998	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
10/208820	JP	24/07/1998	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

☐ Additional foreign application numbers are listed on a supplemental priority sheet attached hereto.

2) PROVISIONAL PRIORITY CLAIM: I hereby claim the benefit under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

Provisional Application Number(s)	Filing Date (dd/mm/yyyy)

☐ Additional provisional application numbers are listed on a supplemental priority sheet attached hereto.

3) U.S./PCT PRIORITY CLAIM: I hereby claim the benefit under Title 35, United States Code, §120 of any United States application or §365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

POWER OF ATTORNEY:

As a named inventor, I hereby appoint the following attorneys and/or agents to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

James E. Cockfield	Reg. No. <u>19,162</u>	Peter C. Lauro	Reg. No. <u>32,360</u>
Thomas V. Smurzynski	Reg. No. <u>24,798</u>	DeAnn F. Smith	Reg. No. <u>36,683</u>
Ralph A. Loren	Reg. No. <u>29,325</u>	David J. Rikkers	Reg. No. <u>43,882</u>
Giulio A. DeConti, Jr.	Reg. No. <u>31,503</u>	Chi Suk Kim	Reg. No. <u>42,728</u>
Ann Lamport Hammitte	Reg. No. <u>34,858</u>	Maria Laccotripe Zacharakis	Limited Recognition Under 37 C.F.R. § 10.9(b)
Elizabeth A. Hanley	Reg. No. <u>33,505</u>		
Amy E. Mandragouras	Reg. No. <u>36,207</u>	Debra J. Milasincic	Reg. No. <u>46,931</u>
Anthony A. Laurentano	Reg. No. <u>38,220</u>	David R. Burns	Reg. No. <u>46,590</u>
Jane E. Remillard	Reg. No. <u>38,872</u>	Sean D. Detweiler	Reg. No. <u>42,482</u>
Jeremiah Lynch	Reg. No. <u>17,425</u>	Peter S. Stecher	Reg. No. <u>37,259</u>
Kevin J. Canning	Reg. No. <u>35,470</u>	Adam M. Goodman	Reg. No. <u>43,640</u>
Jeanne M. DiGiorgio	Reg. No. <u>41,710</u>	Cynthia L. Kanik	Reg. No. <u>37,320</u>
Megan E. Williams	Reg. No. <u>43,270</u>		
Nicholas P. Triano III	Reg. No. <u>36,397</u>		

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Barbara A. Gyure	Reg. No. <u>34,614</u>	Elizabeth A. Hurley	Reg. No. <u>41,859</u>

of GENETICS INSTITUTE, INC., 87 CambridgePark Drive, Cambridge, Massachusetts 02140, United States of America,

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Gale F. Matthews	Reg. No. <u>32,269</u>	Alan M. Gordon	Reg. No. <u>30,637</u>
Darryl L. Webster	Reg. No. <u>34,276</u>		

of GENETICS INSTITUTE, INC., One Campus Drive, Parsippany, New Jersey 07054, United States of America, and

Rebecca R. Barrett	Reg. No. <u>35,152</u>	Steven R. Eck	Reg. No. <u>36,126</u>
Arnold S. Milowsky	Reg. No. <u>35,288</u>	Michael R. Nagy	Reg. No. <u>33,432</u>
George Tarnowski	Reg. No. <u>27,472</u>		

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Send Correspondence to: Amy E. Mandragouras, Esq., Lahive & Cockfield, LLP, 28 State Street, Boston, Massachusetts 02109, United States of America

Direct Telephone Calls to: Amy E. Mandragouras, Esq., (617) 227-7400, Lahive & Cockfield, LLP, 28 State Street, Boston, Massachusetts 02109, United States of America

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Wherefore, I petition that letters patent be granted to me for the invention or discovery described and claimed in the attached specification and claims, and hereby subscribe my name to said specification and claims and to the foregoing declaration, power of attorney, and this petition.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor Seishi KATO	
Inventor's signature <i>Seishi Kato</i>	Date 29. Mar. 2001
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Citizenship Japan	
Post Office Address (if different)	

Full name of sole or first inventor Tomoko KIMURA	
Inventor's signature <i>Tomoko Kimura</i>	Date 27. Apr. 2001
Residence 715, 2-9-1, Kohoku, Tsuchiura-shi, Ibaraki 300-0032, Japan JPX	
Citizenship Japan	
Post Office Address (if different)	

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (dd/mm/yyyy)	Parent Patent Number (if applicable)
	PCT/JP99/03929	22 July 1999 (22.07.99)	

☐ Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto.



ENTERED

PCT09

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 7 <141> CURRENT FILING DATE: 1999-07-22
 8 <150> PRIOR APPLICATION NUMBER: JP 10-208820
 9 <151> PRIOR FILING DATE: 1998-07-24
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 17 <151> PRIOR FILING DATE: 1998-09-29
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 28 20 25 30
 29 Ala Ala Ala Asp Ala Arg Gly Arg Ala Gly His Arg Ser Ala Ala Ala
 30 35 40 45
 31 Ser Asn Leu Ser Gly Leu Ser Leu Gln Glu Ala Gln Gln Ile Leu Asn
 32 50 55 60
 33 Val Ser Lys Leu Ser Pro Glu Glu Val Gln Lys Asn Tyr Glu His Leu
 34 65 70 75 80
 35 Phe Lys Val Asn Asp Lys Ser Val Gly Gly Ser Phe Tyr Leu Gln Ser
 36 85 90 95
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49   20       25       30
50 Tyr Trp Pro Leu Phe Val Leu Phe Tyr Ile Leu Ser Pro Ile Pro
51   35       40       45
52 Tyr Cys Ile Ala Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn
53   50       55       60
54 Ala Cys Lys Glu Leu Ala Ile Phe Leu Thr Thr Gly Ile Val Val Ser
55   65       70       75
56 Ala Phe Gly Leu Pro Ile Val Phe Ala Arg Ala His Leu Ile Glu Trp
57   85       90       95
58 Gly Ala Cys Ala Leu Val Leu Thr Gly Asn Thr Val Ile Phe Ala Thr
59   100      105      110
60 Ile Leu Gly Phe Phe Leu Val Phe Gly Ser Asn Asp Asp Phe Ser Trp
61   115      120      125
62 Gln Gln Trp
63   130

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64 <210> SEQ ID NO: 3

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66 <212> TYPE: PRT

67 <213> ORGANISM: Homo sapiens

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72   20       25       30
73 Arg Asn Pro Ser Asp Arg Lys Val Cys Phe Lys Val Lys Thr Thr Ala
74   35       40       45
75 Pro Arg Arg Tyr Cys Val Arg Pro Asn Ser Gly Ile Ile Asp Pro Gly
76   50       55       60
77 Ser Thr Val Thr Val Ser Val Met Leu Gln Pro Phe Asp Tyr Asp Pro
78   65       70       75
79 Asn Glu Lys Ser Lys His Lys Phe Met Val Gln Thr Ile Phe Ala Pro
80   85       90       95
81 Pro Asn Thr Ser Asp Met Glu Ala Val Trp Lys Glu Ala Lys Pro Asp
82   100      105      110
83 Glu Leu Met Asp Ser Lys Leu Arg Cys Val Phe Glu Met Pro Asn Glu
84   115      120      125
85 Asn Asp Lys Leu Asn Asp Met Glu Pro Ser Lys Ala Val Pro Leu Asn
86   130      135      140
87 Ala Ser Lys Gln Asp Gly Pro Met Pro Lys Pro His Ser Val Ser Leu
88   145      150      155
89 Asn Asp Thr Glu Thr Arg Lys Leu Met Glu Glu Cys Lys Arg Leu Gln
90   165      170      175
91 Gly Glu Met Met Lys Leu Ser Glu Glu Asn Arg His Leu Arg Asp Glu
92   180      185      190
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97 Leu Val Val Ile Ala Ala Ile Phe Ile Gly Phe Phe Leu Gly Lys Phe
98 225          230          235          240
99 Ile Leu
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108      20          25          30
109 Asp Leu Ile Ile Ser Thr Leu Asn Met Ser Lys Ile Gly Tyr Phe Tyr
110      35          40          45
111 Thr Asp Cys Leu Val Pro Met Val Gly Asn Asn Pro Tyr Ala Thr Thr
112      50          55          60
113 Glu Gly Asn Ser Thr Glu Leu Ser Ile Asn Ala Glu Val Tyr Ser Leu
114      65          70          75          80
115 Pro Ser Arg Lys Leu Val Ala Leu Gln Leu Arg Ser Ile Phe Ile Lys
116      85          90          95
117 Tyr Lys Ser Lys Pro Phe Cys Glu Lys Leu Leu Ser Trp Val Lys Ser
118      100          105          110
119 Ser Gly Cys Ala Arg Val Ile Val Leu Ser Ser Ser His Ser Tyr Gln
120      115          120          125
121 Arg Asn Asp Leu Gln Leu Arg Ser Thr Pro Phe Arg Tyr Leu Leu Thr
122      130          135          140
123 Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn Trp
124 145          150          155          160
125 Glu Glu Met Glu Lys Ser Arg Cys Ile Pro Glu Ile Asp Asp Ser Glu
126      165          170          175
127 Phe Cys Ile Arg Ile Pro Gly Gly Gly Ile Thr Lys Thr Leu Tyr Asp
128      180          185          190
129 Glu Ser Cys Ser Lys Glu Ile Gln Met Ala Val Leu Leu Lys Phe Val
130      195          200          205
131 Ser Glu Gly Asp Asn Ile Pro Asp Ala Leu Gly Leu Val Glu Tyr Leu
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133 Asn Glu Trp Leu Gln Ile Leu Lys Pro Leu Ser Asp Asp Pro Thr Val
134 225          230          235          240
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147   20          25          30
148 Gly Ala Pro Thr Ser Pro Ala Glu His Arg Leu Leu Lys Thr Cys Trp
149   35          40          45
150 Ser Cys Arg Val Leu Ser Gly Leu Gly Leu Met Gly Ala Gly Gly Tyr
151   50          55          60
152 Val Tyr Trp Val Ala Arg Lys Pro Met Lys Met Gly Tyr Pro Pro Ser
153   65          70          75          80
154 Pro Trp Thr Thr Ile Thr Gln Met Val Ile Gly Leu Ser Ile Ala Thr Trp
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157  100          105          110

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158 <210> SEQ ID NO: 6

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166   20          25          30
167 Pro Val Gln Glu Glu Lys Leu Ser Ala Ser Thr Ser Asn Leu Pro Cys
168   35          40          45
169 Trp Leu Val Glu Glu Phe Val Val Ala Glu Glu Cys Ser Pro Cys Ser
170   50          55          60
171 Asn Phe Arg Ala Lys Thr Thr Pro Glu Cys Gly Pro Thr Gly Tyr Val
172   65          70          75          80
173 Glu Lys Ile Thr Cys Ser Ser Ser Lys Arg Asn Glu Phe Lys Ser Cys
174   85          90          95
175 Arg Ser Ala Leu Met Glu Gln Arg Leu Phe Trp Lys Phe Glu Gly Ala
176  100          105          110
177 Val Val Cys Val Ala Leu Ile Phe Ala Cys Leu Val Ile Ile Arg Gln
178  115          120          125
179 Arg Gln Leu Asp Arg Lys Ala Leu Glu Lys Val Arg Lys Gln Ile Glu
180  130          135          140
181 Ser Ile
182 145

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183 <210> SEQ ID NO: 7

184 <211> LENGTH: 344

185 <212> TYPE: PRT

186 <213> ORGANISM: Homo sapiens

W--> 187 <400> SEQUENCE: 7

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188 Met Asp Phe Leu Val Leu Phe Leu Tyr Leu Ala Ser Val Leu Met
189   1          5          10          15
190 Gly Leu Val Leu Ile Cys Val Cys Ser Lys Thr His Ser Leu Lys Gly
191  20          25          30

```

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/743,247A

DATE: 11/19/2002

TIME: 14:43:12

Input Set : A:\sequence listing.txt

Output Set : N:\CRF4\11192002\I743247A.raw

```

192 Leu Ala Arg Gly Gly Ala Gln Ile Phe Ser Cys Ile Ile Pro Glu Cys
193      35      40      45
194 Leu Gln Arg Ala Val His Gly Leu Leu His Tyr Leu Phe His Thr Arg
195      50      55      60
196 Asn His Thr Phe Ile Val Leu His Leu Val Leu Gln Gly Met Val Tyr
197      65      70      75      80
198 Thr Glu Tyr Thr Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu
199      85      90      95
200 Ser Leu His Tyr Leu Leu Leu Pro Tyr Leu Leu Leu Gly Val Asn Leu
201      100      105      110
202 Phe Phe Phe Thr Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys
203      115      120      125
204 Ala Asn Glu Leu Leu Phe Leu His Val Tyr Glu Phe Asp Glu Val Met
205      130      135      140
206 Phe Pro Lys Asn Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala
207      145      150      155      160
208 Arg Ser Lys His Cys Ser Val Cys Asn Trp Cys Val His Arg Phe Asp
209      165      170      175
210 His His Cys Val Trp Val Asn Asn Cys Ile Gly Ala Trp Asn Ile Arg
211      180      185      190
212 Tyr Phe Leu Ile Tyr Val Leu Thr Leu Thr Ala Ser Ala Ala Thr Val
213      195      200      205
214 Ala Ile Val Ser Thr Thr Phe Leu Val His Leu Val Val Met Ser Asp
215      210      215      220
216 Leu Tyr Gln Glu Thr Tyr Ile Asp Asp Leu Gly His Leu His Val Met
217      225      230      235      240
218 Asp Thr Val Phe Leu Ile Gln Tyr Leu Phe Leu Thr Phe Pro Arg Ile
219      245      250      255
220 Val Phe Met Leu Gly Phe Val Val Val Leu Ser Phe Leu Leu Gly Gly
221      260      265      270
222 Tyr Leu Leu Phe Val Leu Tyr Leu Ala Ala Thr Asn Gln Thr Thr Asn
223      275      280      285
224 Glu Trp Tyr Arg Gly Asp Trp Ala Trp Cys Gln Arg Cys Pro Leu Val
225      290      295      300
226 Ala Trp Pro Pro Ser Ala Glu Pro Gln Val His Arg Asn Ile His Ser
227      305      310      315      320
228 His Gly Leu Arg Ser Asn Leu Gln Glu Ile Phe Leu Pro Ala Phe Pro
229      325      330      335
230 Cys His Glu Arg Lys Lys Gln Glu
231      340
232 <210> SEQ ID NO: 8
233 <211> LENGTH: 97
234 <212> TYPE: PRT
235 <213> ORGANISM: Homo sapiens
W--> 236 <400> SEQUENCE: 8
237 Met Thr Lys Lys Lys Arg Glu Asn Leu Gly Val Ala Leu Glu Ile Asp
238      1      5      10      15
239 Gly Leu Glu Glu Lys Leu Ser Gln Cys Arg Arg Asp Leu Glu Ala Val
240      20      25      30

```

RAW SEQUENCE LISTING ERROR SUMMARY
PATENT APPLICATION: US/09/743,247A

DATE: 11/19/2002
TIME: 14:43:13

Input Set : A:\sequence listing.txt
Output Set: N:\CRF4\11192002\I743247A.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:93; Xaa Pos. 49
Seq#:113; Xaa Pos. 49

VERIFICATION SUMMARY

DATE: 11/19/2002

PATENT APPLICATION: US/09/743,247A

TIME: 14:43:13

Input Set : A:\sequence listing.txt

Output Set : N:\CRF4\11192002\I743247A.raw

L:3 M:283 W: Missing Blank Line separator, <120> field identifier
L:5 M:283 W: Missing Blank Line separator, <130> field identifier
L:6 M:283 W: Missing Blank Line separator, <140> field identifier
L:18 M:283 W: Missing Blank Line separator, <160> field identifier
L:20 M:283 W: Missing Blank Line separator, <210> field identifier
L:24 M:283 W: Missing Blank Line separator, <400> field identifier
L:45 M:283 W: Missing Blank Line separator, <400> field identifier
L:68 M:283 W: Missing Blank Line separator, <400> field identifier
L:104 M:283 W: Missing Blank Line separator, <400> field identifier
L:143 M:283 W: Missing Blank Line separator, <400> field identifier
L:162 M:283 W: Missing Blank Line separator, <400> field identifier
L:187 M:283 W: Missing Blank Line separator, <400> field identifier
L:236 M:283 W: Missing Blank Line separator, <400> field identifier
L:254 M:283 W: Missing Blank Line separator, <400> field identifier
L:275 M:283 W: Missing Blank Line separator, <400> field identifier
L:322 M:283 W: Missing Blank Line separator, <400> field identifier
L:334 M:283 W: Missing Blank Line separator, <400> field identifier
L:346 M:283 W: Missing Blank Line separator, <400> field identifier
L:364 M:283 W: Missing Blank Line separator, <400> field identifier
L:383 M:283 W: Missing Blank Line separator, <400> field identifier
L:394 M:283 W: Missing Blank Line separator, <400> field identifier
L:407 M:283 W: Missing Blank Line separator, <400> field identifier
L:430 M:283 W: Missing Blank Line separator, <400> field identifier
L:440 M:283 W: Missing Blank Line separator, <400> field identifier
L:452 M:283 W: Missing Blank Line separator, <400> field identifier
L:474 M:283 W: Missing Blank Line separator, <220> field identifier
L:477 M:283 W: Missing Blank Line separator, <400> field identifier
L:508 M:283 W: Missing Blank Line separator, <220> field identifier
L:511 M:283 W: Missing Blank Line separator, <400> field identifier
L:548 M:283 W: Missing Blank Line separator, <220> field identifier
L:551 M:283 W: Missing Blank Line separator, <400> field identifier
L:619 M:283 W: Missing Blank Line separator, <220> field identifier
L:622 M:283 W: Missing Blank Line separator, <400> field identifier
L:683 M:283 W: Missing Blank Line separator, <220> field identifier
L:686 M:283 W: Missing Blank Line separator, <400> field identifier
L:719 M:283 W: Missing Blank Line separator, <220> field identifier
L:722 M:283 W: Missing Blank Line separator, <400> field identifier
L:766 M:283 W: Missing Blank Line separator, <220> field identifier
L:769 M:283 W: Missing Blank Line separator, <400> field identifier
L:826 M:112 C: (48) String data converted to lower case,
L:847 M:283 W: Missing Blank Line separator, <220> field identifier
L:850 M:283 W: Missing Blank Line separator, <400> field identifier
L:880 M:283 W: Missing Blank Line separator, <220> field identifier
L:883 M:283 W: Missing Blank Line separator, <400> field identifier
L:917 M:283 W: Missing Blank Line separator, <220> field identifier
L:920 M:283 W: Missing Blank Line separator, <400> field identifier
L:992 M:283 W: Missing Blank Line separator, <400> field identifier
L:1037 M:283 W: Missing Blank Line separator, <400> field identifier

VERIFICATION SUMMARY

PATENT APPLICATION: US/09/743,247A

DATE: 11/19/2002

TIME: 14:43:13

Input Set : A:\sequence listing.txt

Output Set: N:\CRF4\11192002\I743247A.raw

L:1072 M:283 W: Missing Blank Line separator, <400> field identifier
L:1137 M:283 W: Missing Blank Line separator, <400> field identifier
L:1155 M:283 W: Missing Blank Line separator, <400> field identifier
L:3363 M:257 W: Feature value mis-spelled or invalid, <221> Name/Key for SEQ ID#:93
L:3373 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:93 after pos.:48
L:4053 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ ID#:113
L:4053 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:113 after pos.:198

09/743247

PCT/JP99/03929

WO 00/05367

1/177 534 Rec'd PCT/PTO 05 JAN2001

Sequence listing

<110> Sagami Chemical Research Center; Protegene Inc.

5 <120> Human Proteins Having Hydrophobic Domains And DNAs Encoding These Proteins

<130> 661102

10 <150> JP 10-208820

<151> 1998-07-24

<150> JP 10-224105

<151> 1998-08-07

15

<150> JP 10-238116

<151> 1998-08-25

<150> JP 10-254736

20 <151> 1998-09-09

<150> JP 10-275505

<151> 1998-09-29

25 <160> 150

<170> Windows 95 (Word 98)

<210> 1

30 <211> 125

<212> PRT

<213> Homo sapiens

<400> 1

35 Met Ala Lys Tyr Leu Ala Gln Ile Ile Val Met Gly Val Gln Val Val

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1 5 10 15
 Gly Arg Ala Phe Ala Arg Ala Leu Arg Gln Glu Phe Ala Ala Ser Arg
 20 25 30
 Ala Ala Ala Asp Ala Arg Gly Arg Ala Gly His Arg Ser Ala Ala Ala
 5 35 40 45
 Ser Asn Leu Ser Gly Leu Ser Leu Gln Glu Ala Gln Ile Leu Asn
 50 55 60
 Val Ser Lys Leu Ser Pro Glu Glu Val Gln Lys Asn Tyr Glu His Leu
 65 70 75 80
 10 Phe Lys Val Asn Asp Lys Ser Val Gly Gly Ser Phe Tyr Leu Gln Ser
 85 90 95
 Lys Val Val Arg Ala Lys Glu Arg Leu Asp Glu Glu Leu Lys Ile Gln
 100 105 110
 Ala Gln Glu Asp Arg Glu Lys Gly Gln Met Pro His Thr
 15 115 120 125

<210> 2

<211> 131

<212> PRT

20 <213> Homo sapiens

<400> 2

Met Ala Gly Ile Lys Ala Leu Ile Ser Leu Ser Phe Gly Gly Ala Ile
 1 5 10 15
 25 Gly Leu Met Phe Leu Met Leu Gly Cys Ala Leu Pro Ile Tyr Asn Lys
 20 25 30
 Tyr Trp Pro Leu Phe Val Leu Phe Phe Tyr Ile Leu Ser Pro Ile Pro
 35 40 45
 Tyr Cys Ile Ala Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn
 30 50 55 60
 Ala Cys Lys Glu Leu Ala Ile Phe Leu Thr Thr Gly Ile Val Val Ser
 65 70 75 80
 Ala Phe Gly Leu Pro Ile Val Phe Ala Arg Ala His Leu Ile Glu Trp
 85 90 95
 35 Gly Ala Cys Ala Leu Val Leu Thr Gly Asn Thr Val Ile Phe Ala Thr

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100 105 110
 Ile Leu Gly Phe Phe Leu Val Phe Gly Ser Asn Asp Asp Phe Ser Trp
 115 120 125
 Gln Gln Trp
 5 130
 <210> 3
 <211> 242
 <212> PRT
 10 <213> Homo sapiens
 <400> 3
 Met Ala Lys His Glu Gln Ile Leu Val Leu Asp Pro Pro Thr Asp Leu
 1 5 10 15
 15 Lys Phe Lys Gly Pro Phe Thr Asp Val Val Thr Thr Asn Leu Lys Leu
 20 25 30
 Arg Asn Pro Ser Asp Arg Lys Val Cys Phe Lys Val Lys Thr Thr Ala
 35 40 45
 Pro Arg Arg Tyr Cys Val Arg Pro Asn Ser Gly Ile Ile Asp Pro Gly
 20 50 55 60
 Ser Thr Val Thr Val Ser Val Met Leu Gln Pro Phe Asp Tyr Asp Pro
 65 70 75 80
 Asn Glu Lys Ser Lys His Lys Phe Met Val Gln Thr Ile Phe Ala Pro
 85 90 95
 25 Pro Asn Thr Ser Asp Met Glu Ala Val Trp Lys Glu Ala Lys Pro Asp
 100 105 110
 Glu Leu Met Asp Ser Lys Leu Arg Cys Val Phe Glu Met Pro Asn Glu
 115 120 125
 Asn Asp Lys Leu Asn Asp Met Glu Pro Ser Lys Ala Val Pro Leu Asn
 30 130 135 140
 Ala Ser Lys Gln Asp Gly Pro Met Pro Lys Pro His Ser Val Ser Leu
 145 150 155 160
 Asn Asp Thr Glu Thr Arg Lys Leu Met Glu Glu Cys Lys Arg Leu Gln
 165 170 175
 35 Gly Glu Met Met Lys Leu Ser Glu Glu Asn Arg His Leu Arg Asp Glu

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180 185 190
 Gly Leu Arg Leu Arg Lys Val Ala His Ser Asp Lys Pro Gly Ser Thr
 195 200 205
 Ser Thr Ala Ser Phe Arg Asp Asn Val Thr Ser Pro Leu Pro Ser Leu
 5 210 215 220
 Leu Val Val Ile Ala Ala Ile Phe Ile Gly Phe Phe Leu Gly Lys Phe
 225 230 235 240
 Ile Leu

10 <210> 4
 <211> 264
 <212> PRT
 <213> Homo sapiens

15 <400> 4
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 1 5 10 15
 Leu Leu Met Pro Ala Val Ser Val Gly Asn Val Gly Gln Leu Ala Met
 20 25 30
 20 Asp Leu Ile Ile Ser Thr Leu Asn Met Ser Lys Ile Gly Tyr Phe Tyr
 35 40 45
 Thr Asp Cys Leu Val Pro Met Val Gly Asn Asn Pro Tyr Ala Thr Thr
 50 55 60
 Glu Gly Asn Ser Thr Glu Leu Ser Ile Asn Ala Glu Val Tyr Ser Leu
 25 65 70 75 80
 Pro Ser Arg Lys Leu Val Ala Leu Gln Leu Arg Ser Ile Phe Ile Lys
 85 90 95
 Tyr Lys Ser Lys Pro Phe Cys Glu Lys Leu Leu Ser Trp Val Lys Ser
 100 105 110
 30 Ser Gly Cys Ala Arg Val Ile Val Leu Ser Ser Ser His Ser Tyr Gln
 115 120 125
 Arg Asn Asp Leu Gln Leu Arg Ser Thr Pro Phe Arg Tyr Leu Leu Thr
 130 135 140
 Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn Trp
 35 145 150 155 160

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Glu Glu Met Glu Lys Ser Arg Cys Ile Pro Glu Ile Asp Asp Ser Glu
 165 170 175
 Phe Cys Ile Arg Ile Pro Gly Gly Gly Ile Thr Lys Thr Leu Tyr Asp
 180 185 190
 5 Glu Ser Cys Ser Lys Glu Ile Gln Met Ala Val Leu Leu Lys Phe Val
 195 200 205
 Ser Glu Gly Asp Asn Ile Pro Asp Ala Leu Gly Leu Val Glu Tyr Leu
 210 215 220
 Asn Glu Trp Leu Gln Ile Leu Lys Pro Leu Ser Asp Asp Pro Thr Val
 10 225 230 235 240
 Ser Ala Ser Arg Trp Lys Ile Pro Ser Ser Trp Arg Leu Leu Phe Gly
 245 250 255
 Ser Gly Leu Pro Pro Ala Leu Phe
 260
 15
 <210> 5
 <211> 112
 <212> PRT
 <213> Homo sapiens
 20
 <400> 5
 Met Gly Ser Arg Leu Ser Gln Pro Phe Glu Ser Tyr Ile Thr Ala Pro
 1 5 10 15
 Pro Gly Thr Ala Ala Ala Pro Ala Lys Pro Ala Pro Pro Ala Thr Pro
 25 20 25 30
 Gly Ala Pro Thr Ser Pro Ala Glu His Arg Leu Leu Lys Thr Cys Trp
 35 40 45
 Ser Cys Arg Val Leu Ser Gly Leu Gly Leu Met Gly Ala Gly Gly Tyr
 50 55 60
 30 Val Tyr Trp Val Ala Arg Lys Pro Met Lys Met Gly Tyr Pro Pro Ser
 65 70 75 80
 Pro Trp Thr Ile Thr Gln Met Val Ile Gly Leu Ser Ile Ala Thr Trp
 85 90 95
 Gly Ile Val Val Met Ala Asp Pro Lys Gly Lys Ala Tyr Arg Val Val
 35 100 105 110

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<210> 6

<211> 146

<212> PRT

5 <213> Homo sapiens

<400> 6

Met Leu Ala Gly Ala Gly Arg Pro Gly Leu Pro Gln Gly Arg His Leu

1

5

10

15

10 Cys Trp Leu Leu Cys Ala Phe Thr Leu Lys Leu Cys Gln Ala Glu Ala

20

25

30

Pro Val Gln Glu Glu Lys Leu Ser Ala Ser Thr Ser Asn Leu Pro Cys

35

40

45

Trp Leu Val Glu Glu Phe Val Val Ala Glu Glu Cys Ser Pro Cys Ser

15

50

55

60

Asn Phe Arg Ala Lys Thr Thr Pro Glu Cys Gly Pro Thr Gly Tyr Val

65

70

75

80

Glu Lys Ile Thr Cys Ser Ser Ser Lys Arg Asn Glu Phe Lys Ser Cys

85

90

95

20 Arg Ser Ala Leu Met Glu Gln Arg Leu Phe Trp Lys Phe Glu Gly Ala

100

105

110

Val Val Cys Val Ala Leu Ile Phe Ala Cys Leu Val Ile Ile Arg Gln

115

120

125

Arg Gln Leu Asp Arg Lys Ala Leu Glu Lys Val Arg Lys Gln Ile Glu

25

130

135

140

Ser Ile

145

<210> 7

30 <211> 344

<212> PRT

<213> Homo sapiens

<400> 7

35 Met Asp Phe Leu Val Leu Phe Leu Phe Tyr Leu Ala Ser Val Leu Met

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	1	5	10	15
	Gly Leu Val Leu Ile Cys Val Cys Ser Lys Thr His Ser Leu Lys Gly			
	20	25	30	
	Leu Ala Arg Gly Gly Ala Gln Ile Phe Ser Cys Ile Ile Pro Glu Cys			
5	35	40	45	
	Leu Gln Arg Ala Val His Gly Leu Leu His Tyr Leu Phe His Thr Arg			
	50	55	60	
	Asn His Thr Phe Ile Val Leu His Leu Val Leu Gln Gly Met Val Tyr			
	65	70	75	80
10	Thr Glu Tyr Thr Trp Glu Val Phe Gly Tyr Cys Gln Glu Leu Glu Leu			
	85	90	95	
	Ser Leu His Tyr Leu Leu Leu Pro Tyr Leu Leu Leu Gly Val Asn Leu			
	100	105	110	
	Phe Phe Phe Thr Leu Thr Cys Gly Thr Asn Pro Gly Ile Ile Thr Lys			
15	115	120	125	
	Ala Asn Glu Leu Leu Phe Leu His Val Tyr Glu Phe Asp Glu Val Met			
	130	135	140	
	Phe Pro Lys Asn Val Arg Cys Ser Thr Cys Asp Leu Arg Lys Pro Ala			
	145	150	155	160
20	Arg Ser Lys His Cys Ser Val Cys Asn Trp Cys Val His Arg Phe Asp			
	165	170	175	
	His His Cys Val Trp Val Asn Asn Cys Ile Gly Ala Trp Asn Ile Arg			
	180	185	190	
	Tyr Phe Leu Ile Tyr Val Leu Thr Leu Thr Ala Ser Ala Ala Thr Val			
25	195	200	205	
	Ala Ile Val Ser Thr Thr Phe Leu Val His Leu Val Val Met Ser Asp			
	210	215	220	
	Leu Tyr Gln Glu Thr Tyr Ile Asp Asp Leu Gly His Leu His Val Met			
	225	230	235	240
30	Asp Thr Val Phe Leu Ile Gln Tyr Leu Phe Leu Thr Phe Pro Arg Ile			
	245	250	255	
	Val Phe Met Leu Gly Phe Val Val Val Leu Ser Phe Leu Leu Gly Gly			
	260	265	270	
	Tyr Leu Leu Phe Val Leu Tyr Leu Ala Ala Thr Asn Gln Thr Thr Asn			
35	275	280	285	

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Glu Trp Tyr Arg Gly Asp Trp Ala Trp Cys Gln Arg Cys Pro Leu Val
 290 295 300
 Ala Trp Pro Pro Ser Ala Glu Pro Gln Val His Arg Asn Ile His Ser
 305 310 315 320
 5 His Gly Leu Arg Ser Asn Leu Gln Glu Ile Phe Leu Pro Ala Phe Pro
 325 330 335
 Cys His Glu Arg Lys Lys Gln Glu
 340

10 <210> 8
 <211> 97
 <212> PRT
 <213> Homo sapiens

15 <400> 8
 Met Thr Lys Lys Lys Arg Glu Asn Leu Gly Val Ala Leu Glu Ile Asp
 1 5 10 15
 Gly Leu Glu Glu Lys Leu Ser Gln Cys Arg Arg Asp Leu Glu Ala Val
 20 25 30
 20 Asn Ser Arg Leu His Ser Arg Glu Leu Ser Pro Glu Ala Arg Arg Ser
 35 40 45
 Leu Glu Lys Glu Lys Asn Ser Leu Met Asn Lys Ala Ser Asn Tyr Glu
 50 55 60
 Lys Glu Leu Lys Phe Leu Arg Gln Glu Asn Arg Lys Asn Met Leu Leu
 25 65 70 75 80
 Ser Val Ala Ile Phe Ile Leu Leu Thr Leu Val Tyr Ala Tyr Trp Thr
 85 90 95
 Met

30 <210> 9
 <211> 124
 <212> PRT
 <213> Homo sapiens

35 <400> 9

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Met Ala Thr Ser Ser Met Ser Lys Gly Cys Phe Val Phe Lys Pro Asn
 1 5 10 15
 Ser Lys Lys Arg Lys Ile Ser Leu Pro Ile Glu Asp Tyr Phe Asn Lys
 20 25 30
 5 Gly Lys Asn Glu Pro Glu Asp Ser Lys Leu Arg Phe Glu Thr Tyr Gln
 35 40 45
 Leu Ile Trp Gln Gln Met Lys Ser Glu Asn Glu Arg Leu Gln Glu Glu
 50 55 60
 Leu Asn Lys Asn Leu Phe Asp Asn Leu Ile Glu Phe Leu Gln Lys Ser
 10 65 70 75 80
 His Ser Gly Phe Gln Lys Asn Ser Arg Asp Leu Gly Gly Gln Ile Lys
 85 90 95
 Leu Arg Glu Ile Pro Thr Ala Ala Leu Val Leu Gly Ile Tyr Ala Tyr
 100 105 110
 15 Val Cys Ser Cys Met His Leu Cys Val Phe Arg Phe
 115 120

<210> 10

<211> 327

20 <212> PRT

<213> Homo sapiens

<400> 10

Met Ala Glu Leu Pro Gly Pro Phe Leu Cys Gly Ala Leu Leu Gly Phe
 25 1 5 10 15
 Leu Cys Leu Ser Gly Leu Ala Val Glu Val Lys Val Pro Thr Glu Pro
 20 25 30
 Leu Ser Thr Pro Leu Gly Lys Thr Ala Glu Leu Thr Cys Thr Tyr Ser
 35 40 45
 30 Thr Ser Val Gly Asp Ser Phe Ala Leu Glu Trp Ser Phe Val Gln Pro
 50 55 60
 Gly Lys Pro Ile Ser Glu Ser His Pro Ile Leu Tyr Phe Thr Asn Gly
 65 70 75 80
 His Leu Tyr Pro Thr Gly Ser Lys Ser Lys Arg Val Ser Leu Leu Gln
 35 85 90 95

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Asn Pro Pro Thr Val Gly Val Ala Thr Leu Lys Leu Thr Asp Val His
 100 105 110
 Pro Ser Asp Thr Gly Thr Tyr Leu Cys Gln Val Asn Asn Pro Pro Asp
 115 120 125
 5 Phe Tyr Thr Asn Gly Leu Gly Leu Ile Asn Leu Thr Val Leu Val Pro
 130 135 140
 Pro Ser Asn Pro Leu Cys Ser Gln Ser Gly Gln Thr Ser Val Gly Gly
 145 150 155 160
 Ser Thr Ala Leu Arg Cys Ser Ser Ser Glu Gly Ala Pro Lys Pro Val
 10 165 170 175
 Tyr Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser
 180 185 190
 Met Val Gln Asp Glu Val Ser Gly Gln Leu Ile Leu Thr Asn Leu Ser
 195 200 205
 15 Leu Thr Ser Ser Gly Thr Tyr Arg Cys Val Ala Thr Asn Gln Met Gly
 210 215 220
 Ser Ala Ser Cys Glu Leu Thr Leu Ser Val Thr Glu Pro Ser Gln Gly
 225 230 235 240
 Arg Val Ala Gly Ala Leu Ile Gly Val Leu Leu Gly Val Leu Leu Leu
 20 245 250 255
 Ser Val Ala Ala Phe Cys Leu Val Arg Phe Gln Lys Glu Arg Gly Lys
 260 265 270
 Lys Pro Lys Glu Thr Tyr Gly Gly Ser Asp Leu Arg Glu Asp Ala Ile
 275 280 285
 25 Ala Pro Gly Ile Ser Glu His Thr Cys Met Arg Ala Asp Ser Ser Lys
 290 295 300
 Gly Phe Leu Glu Arg Pro Ser Ser Ala Ser Thr Val Thr Thr Thr Lys
 305 310 315 320
 Ser Lys Leu Pro Met Val Val
 30 325

 <210> 11
 <211> 375
 <212> DNA
 35 <213> Homo sapiens

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<400> 11	
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	gcacgggacct tgcggcagga gtttgacagc agcggggccg cagctgatgc ccgaggacgc 120
5	gctggacacc ggtetgcagc cgcttccaac ctctccggcc tcagcctcca ggaggcacag 180
	cagattctca acgtgtccaa gctgagccct gaggaggtcc agaagaacta tgaacactta 240
	tttaaggtag atgataaatc cgtgggtggc tccttctacc tgcagtcaaa ggtggtccgc 300
	gcaaggagac gcctggatga ggaactcaaa atccaggccc agggaggacag agaaaaaggg 360
	cagatgcccc atacg 375
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<211> 393	
<212> DNA	
<213> Homo sapiens	
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	ttgatgcttg gatgtgccct tccaatatac aacaaatact ggcccccttt tgttctattt 120
	ttttacatcc ttccacctat tccatactgc atagcaagaa gattagtggg tgatacagat 180
20	gctatgagta acgcttgtaa ggaacttgcc atctttctta caacgggcat tgcgtgtgca 240
	gcttttggac tccctattgt atttgccaga gcacatctga ttgagtgggg agcttgtgca 300
	cttgcttcca caggaaacac agtcatcttt gcaactatac taggcttttt cttggtcttt 360
	ggaagcaatg acgaactcag ctggcagcag tgg 393
25	
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<211> 726	
<212> DNA	
<213> Homo sapiens	
30	
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	cccttcacag atgtagtcaac tacaaatctt aaattgcgaa atccatcgga tagaaaagtg 120
	tgtttcaaa gaaagactac agcacctcgc cggtagctgtg tgaggcccaa cagtggaaat 180
	attgacccag ggtcaactgt gactgtttca gtaatgctac agccctttga ctatgatccg 240
35	aatgaaaaga gtaaacacaa gtttatggta cagacaattt ttgctccacc aaacacttca 300

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	gatatggaag	ctgtgtggaa	agaggcaaaa	cctgatgaat	taatggattc	caaattgaga	360
	tgcgtatttg	aaatgcccaa	tgaaaatgat	aaattgaatg	atatggaacc	tagcaaaagct	420
	gttcactga	atgcattcaa	gcaagatgga	cctatgcoaa	aaccacacag	tgtttcactt	480
	aatgataccg	aaacaaggaa	actaatggaa	gagtgtaaaa	gacttcaagg	agaaatgatg	540
5	aagctatcag	aagaaaaatc	gcacctgaga	gatgaaggtt	taaggctcag	aaaggtagca	600
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Met Ala Lys

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 Ser Lys His Lys Phe Met Val Gln Thr Ile Phe Ala Pro Pro Asn Thr

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 Thr Leu Leu Met Pro Ala Val Ser Val Gly Asn Val Gly Gln Leu Ala
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 25 Tyr Thr Asp Cys Leu Val Pro Met Val Gly Asn Asn Pro Tyr Ala Thr
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 Leu Pro Ser Arg Lys Leu Val Ala Leu Gln Leu Arg Ser Ile Phe Ile
 80 85 90 95
 aag tat aaa tca aag cca ttc tgt gaa aaa ctg ctt tcc tgg gtg aaa 397
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Gly Thr Ala Ala Ala Pro Ala Lys Pro Ala Pro Pro Ala Thr Pro Gly
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Ala Pro Thr Ser Pro Ala Glu His Arg Leu Leu Lys Thr Cys Trp Ser
35 40 45
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Cys Arg Val Leu Ser Gly Leu Gly Leu Met Gly Ala Gly Gly Tyr Val
50 55 60 65
25 tac tgg gtg gca cgg aag ccc atg aag atg gga tac ccc ccg agt cca 296
Tyr Trp Val Ala Arg Lys Pro Met Lys Met Gly Tyr Pro Pro Ser Pro
70 75 80
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Trp Thr Ile Thr Gln Met Val Ile Gly Leu Ser Ile Ala Thr Trp Gly
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 15 ggtgagcggg cgctagggcc gcgagccccc gccggccctt cctccagcgc cctgcgggacc 180
 ccgcagaagg cgctgcctc cctagccccc aaaaacatat cgatttttct cgctgtggca 240
 acggggacgt cctgatagat cctctgctcc aataggcaac tccggccttc cctgccctga 300
 cctggaacct ctgggagggc tgcagagtaa gtgccgcctc tgcgctccga cggaggcaag 360
 aggcctgtgg agtaggtccc tctgttccga caggtgcgac acttggcgct cc atg ett 418
 20 Met Leu
 1
 gcg ggt gcc ggg agg cct ggc ctg ccc cag ggc cgc cgc ctg tgc tgg 466
 Ala Gly Ala Gly Arg Pro Gly Leu Pro Gln Gly Arg His Leu Cys Trp
 5 10 15
 25 ttg ctg tgt gct ttc acc tta aag ctg tgc caa gca gag gct ccc gtg 514
 Leu Leu Cys Ala Phe Thr Leu Lys Leu Cys Gln Ala Glu Ala Pro Val
 20 25 30
 cag gaa gag aag ctg tca gca agc acc tca aat ttg cca tgc tgg ctg 562
 Gln Glu Glu Lys Leu Ser Ala Ser Thr Ser Asn Leu Pro Cys Trp Leu
 30 35 40 45 50
 gtg gaa gag ttt gtg gta gca gaa gag tgc tct cca tgc tct aat ttc 610
 Val Glu Glu Phe Val Val Ala Glu Glu Cys Ser Pro Cys Ser Asn Phe
 55 60 65
 cgg gct aaa act acc cct gag tgt ggt ccc aca gga tat gta gag aaa 658
 35 Arg Ala Lys Thr Thr Pro Glu Cys Gly Pro Thr Gly Tyr Val Glu Lys

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	70	75	80	
	atc aca tgc agc tca tct aag aga aat gag ttc aaa agc tgc cgc tca			706
	Ile Thr Cys Ser Ser Ser Lys Arg Asn Glu Phe Lys Ser Cys Arg Ser			
	85	90	95	
5	gct ttg atg gaa caa cgc tta ttt tgg aag ttc gaa ggg gct gtc gtg			754
	Ala Leu Met Glu Gln Arg Leu Phe Trp Lys Phe Glu Gly Ala Val Val			
	100	105	110	
	tgt gtg gcc ctg atc ttc gct tgt ctt gtc atc att cgt cag cga caa			802
	Cys Val Ala Leu Ile Phe Ala Cys Leu Val Ile Ile Arg Gln Arg Gln			
10	115	120	125	130
	ttg gac aga aag gct ctg gaa aag gtc cgg aag caa atc gag tcc ata			850
	Leu Asp Arg Lys Ala Leu Glu Lys Val Arg Lys Gln Ile Glu Ser Ile			
	135	140	145	
	tagctacatt ccacccttgt atcctgggtc ttagagaccc tatctcagac agtgaagtgc			910
15	aaatggactg atttgcactc ttggttcttt ggagccttgc ggtggaatcc ccttttcccc			970
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20	<212> DNA			
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	gcccagatgc gggcgccccc cgggtgtccc tccgagcctg ctgcaactca cgtcccccta			120
	ccagggtccc agcccccagg gaaatctccg accaggcccc ccaggagccc agatccaggc			180
30	tcttggaaga accatgtccg gcagctactg gtcattgccag gcacacactg ctgcccgaaga			240
	ggagctgctg ttggaattat ctgtgaatgt tgggaagagg aatgccagag ctgcggctg			300
	aaaattaccc aaccaagaga aatctgcagg atg gac ttt ctg gtc etc ttc ttg			354
	Met Asp Phe Leu Val Leu Phe Leu			
	1	5		
35	ttc tac ctg gct tcc gtg ctg atg ggt ctt gtt ctt atc tgc gtc tgc			402

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	Phe Tyr Leu Ala Ser Val Leu Met Gly Leu Val Leu Ile Cys Val Cys	
	10 15 20	
	tgc aaa acc cat agc ttg aaa ggc ctg gcc agg gga gga gca cag ata	450
	Ser Lys Thr His Ser Leu Lys Gly Leu Ala Arg Gly Gly Ala Gln Ile	
5	25 30 35 40	
	ttt tcc tgt ata att cca gaa tgt ctt cag aga gcc gtg cat gga ttg	498
	Phe Ser Cys Ile Ile Pro Glu Cys Leu Gln Arg Ala Val His Gly Leu	
	45 50 55	
	ctt cat tac ctt ttc cat acg aga aac cac acc ttc att gtc ctg cac	546
10	Leu His Tyr Leu Phe His Thr Arg Asn His Thr Phe Ile Val Leu His	
	60 65 70	
	ctg gtc ttg caa ggg atg gtt tat act gag tac acc tgg gaa gta ttt	594
	Leu Val Leu Gln Gly Met Val Tyr Thr Glu Tyr Thr Trp Glu Val Phe	
	75 80 85	
15	ggc tac tgt cag gag ctg gag ttg tcc ttg cat tac ctt ctt ctg ccc	642
	Gly Tyr Cys Gln Glu Leu Glu Leu Ser Leu His Tyr Leu Leu Leu Pro	
	90 95 100	
	tat ctg ctg cta ggt gta aac ctg ttt ttt ttc acc ctg act tgt gga	690
	Tyr Leu Leu Leu Gly Val Asn Leu Phe Phe Phe Thr Leu Thr Cys Gly	
20	105 110 115 120	
	acc aat cct ggc att ata aca aaa gca aat gaa tta tta ttt ctt cat	738
	Thr Asn Pro Gly Ile Ile Thr Lys Ala Asn Glu Leu Leu Phe Leu His	
	125 130 135	
	gtt tat gaa ttt gat gaa gtg atg ttt cca aag aac gtg agg tgc tct	786
25	Val Tyr Glu Phe Asp Glu Val Met Phe Pro Lys Asn Val Arg Cys Ser	
	140 145 150	
	act tgt gat tta agg aaa cca gct cga tcc aag cac tgc agt gtg tgt	834
	Thr Cys Asp Leu Arg Lys Pro Ala Arg Ser Lys His Cys Ser Val Cys	
	155 160 165	
30	aac tgg tgt gtg cac cgt ttc gac cat cac tgt gtt tgg gtg aac aac	882
	Asn Trp Cys Val His Arg Phe Asp His His Cys Val Trp Val Asn Asn	
	170 175 180	
	tgc atc ggg gcc tgg aac atc agg tac ttc ctc atc tac gtc ttg acc	930
	Cys Ile Gly Ala Trp Asn Ile Arg Tyr Phe Leu Ile Tyr Val Leu Thr	
35	185 190 195 200	

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	ttg acg gcc tcg gct gcc acc gtc gcc att gtg agc acc act ttt ctg	978
	Leu Thr Ala Ser Ala Ala Thr Val Ala Ile Val Ser Thr Thr Phe Leu	
	205 210 215	
	gtc cac ttg gtg gtg atg tca gat tta tac cag gag act tac atc gat	1026
5	Val His Leu Val Val Met Ser Asp Leu Tyr Gln Glu Thr Tyr Ile Asp	
	220 225 230	
	gac ctt gga cac ctc cat gtt atg gac acg gtc ttt ctt att cag tac	1074
	Asp Leu Gly His Leu His Val Met Asp Thr Val Phe Leu Ile Gln Tyr	
	235 240 245	
10	ctg ttc ctg act ttt cca cgg att gtc ttc atg ctg ggc ttt gtc gtg	1122
	Leu Phe Leu Thr Phe Pro Arg Ile Val Phe Met Leu Gly Phe Val Val	
	250 255 260	
	GTT CTG AGC TTC CTC CTG GGT GGC TAC CTG TTG TTT GTC CTG TAT CTG	1170
	Val Leu Ser Phe Leu Leu Gly Gly Tyr Leu Leu Phe Val Leu Tyr Leu	
15	265 270 275 280	
	gcg gcc acc aac cag act act aac gag tgg tac aga ggt gac tgg gcc	1218
	Ala Ala Thr Asn Gln Thr Thr Asn Glu Trp Tyr Arg Gly Asp Trp Ala	
	285 290 295	
	tgg tgc cag cgt tgt ccc ctt gtg gcc tgg cct ccg tca gca gag ccc	1266
20	Trp Cys Gln Arg Cys Pro Leu Val Ala Trp Pro Pro Ser Ala Glu Pro	
	300 305 310	
	caa gtc cac cgg aac att cac tcc cat ggg ctt cgg agc aac ctt caa	1314
	Gln Val His Arg Asn Ile His Ser His Gly Leu Arg Ser Asn Leu Gln	
	315 320 325	
25	gag atc ttt cta cct gcc ttt cca tgt cat gag agg aag aaa caa gaa	1362
	Glu Ile Phe Leu Pro Ala Phe Pro Cys His Glu Arg Lys Lys Gln Glu	
	330 335 340	
	tgacaagtgt atgaactgct ttgagctgta gttcccggtt atttacacat gtggatcc	1420
	tcgttttcca ag	1432
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	<211> 601	
	<212> DNA	
	<213> Homo sapiens	
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<221> CDS

<222> (62)...(355)

<400> 28

5	atgcgcacat agcgacttgg tgggcgcgtc cagtgatgac tgggggatcc cggcaagtaa	60
	c atg act aaa aag aag cgg gag aat ctg gcc gtc gct cta gag atc gat	109
	Met Thr Lys Lys Lys Arg Glu Asn Leu Gly Val Ala Leu Glu Ile Asp	
	1 5 10 15	
	ggg cta gag gag aag ctg tcc cag tgt cgg aga gac ctg gag gcc gtg	157
10	Gly Leu Glu Glu Lys Leu Ser Gln Cys Arg Arg Asp Leu Glu Ala Val	
	20 25 30	
	aac tcc aga ctc cac agc cgg gag ctg agc cca gag gcc agg agg tcc	205
	Asn Ser Arg Leu His Ser Arg Glu Leu Ser Pro Glu Ala Arg Arg Ser	
	35 40 45	
15	ctg gag aag gag aaa aac agc cta atg aac aaa gcc tcc aac tac gag	253
	Leu Glu Lys Glu Lys Asn Ser Leu Met Asn Lys Ala Ser Asn Tyr Glu	
	50 55 60	
	aag gaa ctg aag ttt ctt cgg caa gag aac cgg aag aac atg ctg ctc	301
	Lys Glu Leu Lys Phe Leu Arg Gln Glu Asn Arg Lys Asn Met Leu Leu	
20	65 70 75 80	
	tct gtg gcc atc ttt atc ctc ctg acg ctc gtc tat gcc tac tgg acc	349
	Ser Val Ala Ile Phe Ile Leu Leu Thr Leu Val Tyr Ala Tyr Trp Thr	
	85 90 95	
	atg tgagcctggc acttcccac aaccagcaca ggetteccact tggcccct	400
25	Met	
	tgatcaggat caagcaggca cttcaagcct caataggacc aaggtgctgg ggtgttcccc	460
	tcccacacta gtgttcaagc atggcttccct ggaggccacc gccttgccctc cotggcctgc	520
	tgggggggttc cgggtctcca gaaggacatg gtgctggtcc ctcccttagc ccaagggaga	580
30	ggcaataaag acacaaagct g	601

<210> 29

<211> 585

<212> DNA

35 <213> Homo sapiens

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<220>

<221> CDS

<222> (78)...(452)

5 <400> 29
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gcagagtcag taagacc atg gct acg tcc tgg atg tct aag ggt tgc ttt 110
Met Ala Thr Ser Ser Met Ser Lys Gly Cys Phe
1 5 10
10 gtt ttt aag cca aac tcc aaa aag aga aag atc tct ctg cca ata gag 158
Val Phe Lys Pro Asn Ser Lys Lys Arg Lys Ile Ser Leu Pro Ile Glu
15 20 25
gac tat ttt aac aaa ggg aaa aat gag cct gag gac agt aag ctt cga 206
Asp Tyr Phe Asn Lys Gly Lys Asn Glu Pro Glu Asp Ser Lys Leu Arg
15 30 35 40
ttc gaa act tat cag ttg ata tgg cag cag atg aaa tct gaa aat gag 254
Phe Glu Thr Tyr Gln Leu Ile Trp Gln Gln Met Lys Ser Glu Asn Glu
45 50 55
cga cta caa gag gaa tta aat aaa aac ttg ttt gac aat ctg att gaa 302
Arg Leu Gln Glu Glu Leu Asn Lys Asn Leu Phe Asp Asn Leu Ile Glu
20 60 65 70 75
ttt ctg caa aaa tca cat tct tga ttc cag aag aat tca aga gac ttg 350
Phe Leu Gln Lys Ser His Ser Gly Phe Gln Lys Asn Ser Arg Asp Leu
80 85 90
25 ggc ggt caa ata aaa ctg aga gaa att cca act gct gct ctt gtt ctt 398
Gly Gly Gln Ile Lys Leu Arg Glu Ile Pro Thr Ala Ala Leu Val Leu
95 100 105
ggg ata tat gcg tat gtt tgt tca tgc atg cat ctg tgt gta ttt cgt 446
Gly Ile Tyr Ala Tyr Val Cys Ser Cys Met His Leu Cys Val Phe Arg
30 110 115 120
ttt taaatttttt ttattgttg agaatagtgg aaggacctgt ttgatgagc c 500
Phe
tattttgtct ctcttatttg tacaattaaa ccaactatag ttatattac atattttcaa 560
35 aaaccaataa aaattcttta ttttt 585

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<210> 30
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 <212> DNA
 5 <213> Homo sapiens
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15 gcc gag ctc ccg ggg ccc ttt ctc tgc ggg gcc ctg cta ggc ttc ctg 107
 Ala Glu Leu Pro Gly Pro Phe Leu Cys Gly Ala Leu Leu Gly Phe Leu
 5 10 15
 tgc ctg agt ggg ctg gcc gtg gag gtg aag gta ccc aca gag ccg ctg 155
 Cys Leu Ser Gly Leu Ala Val Glu Val Lys Val Pro Thr Glu Pro Leu
 20 25 30

20 agc acg ccc ctg ggg aag aca gcc gag ctg acc tgc acc tac agc acg 203
 Ser Thr Pro Leu Gly Lys Thr Ala Glu Leu Thr Cys Thr Tyr Ser Thr
 35 40 45
 tcg gtg gga gac agc ttc gcc ctg gag tgg agc ttt gtg cag cct ggg 251
 Ser Val Gly Asp Ser Phe Ala Leu Glu Trp Ser Phe Val Gln Pro Gly

25 50 55 60 65
 aaa ccc atc tct gag tcc cat cca atc ctg tac ttc acc aat ggc cat 299
 Lys Pro Ile Ser Glu Ser His Pro Ile Leu Tyr Phe Thr Asn Gly His
 70 75 80

30 ctg tat cca act ggt tct aag tca aag cgg gtc agc ctg ctt cag aac 347
 Leu Tyr Pro Thr Gly Ser Lys Ser Lys Arg Val Ser Leu Leu Gln Asn
 85 90 95

ccc ccc aca gtg ggg gtg gcc aca ctg aaa ctg act gac gtc cac ccc 395
 Pro Pro Thr Val Gly Val Ala Thr Leu Lys Leu Thr Asp Val His Pro
 100 105 110

35 tca gat act gga acc tac ctc tgc caa gtc aac aac cca cca gat ttc 443

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	Ser Asp Thr Gly Thr Tyr Leu Cys Gln Val Asn Asn Pro Pro Asp Phe	
	115 120 125	
	tac acc aat ggg ttg ggg cta atc aac ctt act gtg ctg gtt ccc ccc	491
	Tyr Thr Asn Gly Leu Gly Leu Ile Asn Leu Thr Val Leu Val Pro Pro	
5	130 135 140 145	
	agt aat ccc tta tgc agt cag agt gga caa acc tct gtg gga ggc tct	539
	Ser Asn Pro Leu Cys Ser Gln Ser Gly Gln Thr Ser Val Gly Gly Ser	
	150 155 160	
	act gca ctg aga tgc agc tct tcc gag ggg gct cct aag cca gtg tac	587
10	Thr Ala Leu Arg Cys Ser Ser Ser Glu Gly Ala Pro Lys Pro Val Tyr	
	165 170 175	
	aac tgg gtg cgt ctt gga act ttt cct aca cct tct cct ggc agc atg	635
	Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser Met	
	180 185 190	
15	gtt caa gat gag gtg tct ggc cag ctc att ctc acc aac ctc tcc ctg	683
	Val Gln Asp Gly Val Ser Gly Gln Leu Ile Leu Thr Asn Leu Ser Leu	
	195 200 205	
	acc tcc tog ggc acc tac cgc tgt gtg gcc acc aac cag atg ggc agt	731
	Thr Ser Ser Gly Thr Tyr Arg Cys Val Ala Thr Asn Gln Met Gly Ser	
20	210 215 220 225	
	gca tcc tgt gag ctg acc ctc tct gtg acc gaa ccc tcc caa ggc cga	779
	Ala Ser Cys Glu Leu Thr Leu Ser Val Thr Glu Pro Ser Gln Gly Arg	
	230 235 240	
	gtg gcc gga gct ctg att ggg gtg ctc ctg ggc gtg ctg ttg ctg tca	827
25	Val Ala Gly Ala Leu Ile Gly Val Leu Leu Gly Val Leu Leu Ser	
	245 250 255	
	gtt gct gcg ttc tgc ctg gtc agg ttc cag aaa gag agg ggg aag aag	875
	Val Ala Ala Phe Cys Leu Val Arg Phe Gln Lys Glu Arg Gly Lys Lys	
	260 265 270	
30	ccc aag gag aca tat ggg ggt agt gac ctt cgg gag gat gcc atc gct	923
	Pro Lys Glu Thr Tyr Gly Gly Ser Asp Leu Arg Glu Asp Ala Ile Ala	
	275 280 285	
	cct ggg atc tct gag cac act tgt atg agg gct gat tct agc aag ggg	971
	Pro Gly Ile Ser Glu His Thr Cys Met Arg Ala Asp Ser Ser Lys Gly	
35	290 295 300 305	

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ttc ctg gaa aga ccc tgg tet gcc agc acc gtg acg acc acc aag tcc 1019
 Phe Leu Glu Arg Pro Ser Ser Ala Ser Thr Val Thr Thr Thr Lys Ser
 310 315 320
 aag ctc cct atg gtc gtg tgacttctcc cgatccotga gggcggtgag ggg 1070
 5 Lys Leu Pro Met Val Val
 325
 gaatatcaat aattaaagtc tgtgggtacc 1100

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 10 <211> 313
 <212> PRT
 <213> Homo sapiens

 <400> 31
 15 Met Asn Gln Leu Ser Phe Leu Leu Phe Leu Ile Ala Thr Thr Arg Gly
 1 5 10 15
 Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser
 20 25 30
 Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys
 20 35 40 45
 Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val
 50 55 60
 Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr
 65 70 75 80
 25 Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val
 85 90 95
 Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu
 100 105 110
 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala
 30 115 120 125
 Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala
 130 135 140
 Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His
 145 150 155 160
 35 Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu

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165 170 175
 Gln Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val
 180 185 190
 Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro
 5 195 200 205
 Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser
 210 215 220
 Pro Tyr Gly Gln Arg Glu Phe Thr Ala Gly Phe Val Gln Phe Arg Val
 225 230 235 240
 10 Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val
 245 250 255
 Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe
 260 265 270
 Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp
 15 275 280 285
 Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr
 290 295 300
 Glu Ala Ala Val Leu Leu Phe Tyr Arg
 305 310
 20
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 <211> 229
 <212> PRT
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 25
 <400> 32
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 1 5 10 15
 Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu
 30 20 25 30
 Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe
 35 40 45
 Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val
 50 55 60
 35 Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu

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65 70 75 80
 Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr
 85 90 95
 Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe
 5 100 105 110
 Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn
 115 120 125
 Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr
 130 135 140
 10 Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile
 145 150 155 160
 Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu
 165 170 175
 Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe
 15 180 185 190
 Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val
 195 200 205
 Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys
 210 215 220
 20 Arg Lys Ser Arg Thr
 225

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 <211> 467
 25 <212> PRT
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 20 25 30
 Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala
 35 40 45
 35 Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe

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	50		55		60	
	Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Gln Lys					
	65		70		75	80
	Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro					
5		85		90		95
	Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe					
		100		105		110
	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr					
		115		120		125
10	Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser					
		130		135		140
	Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp					
		145		150		155
	Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg					
15		165		170		175
	Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu					
		180		185		190
	Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys					
		195		200		205
20	Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val					
		210		215		220
	Leu Trp Ser Asp Gly Asp Gly Gly Ala Pro Asp Gln Tyr Trp Asn Ser					
		225		230		235
	Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr					
25		245		250		255
	Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly					
		260		265		270
	Gly Phe Tyr Trp Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro					
		275		280		285
30	His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr					
		290		295		300
	Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val					
		305		310		315
	Lys Gln Leu Val Glu Thr Val Ser Cys Gly Asn Leu Leu Met Asn					
35		325		330		335

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Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg
340 345 350
Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr
355 360 365
5 Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val
370 375 380
Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu
385 390 395 400
Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile
10 405 410 415
Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn
420 425 430
Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu
435 440 445
15 Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr
450 455 460
Asn Val Ile
465
20 <210> 34
<211> 99
<212> PRT
<213> Homo sapiens
25 <400> 34
Met Asp Asn Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser
1 5 10 15
Val Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu
20 25 30
30 Val Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro
35 40 45
Glu Thr Thr Thr Leu Thr Val Gly Gly Gly Val Phe Ala Leu Val Thr
50 55 60
Ala Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu
35 65 70 75 80

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Phe Asn Pro Ser Gly Pro Tyr Gln Gln Lys Pro Val His Glu Lys Lys
85 90 95
Glu Val Leu

5 <210> 35
<211> 189
<212> PRT
<213> Homo sapiens

10 <400> 35
Met Glu Glu Gly Gly Asn Leu Gly Gly Leu Ile Lys Met Val His Leu
1 5 10 15
Leu Val Leu Ser Gly Ala Trp Gly Met Gln Met Trp Val Thr Phe Val
20 25 30

15 Ser Gly Phe Leu Leu Phe Arg Ser Leu Pro Arg His Thr Phe Gly Leu
35 40 45
Val Gln Ser Lys Leu Phe Pro Phe Tyr Phe His Ile Ser Met Gly Cys
50 55 60
Ala Phe Ile Asn Leu Cys Ile Leu Ala Ser Gln His Ala Trp Ala Gln
20 65 70 75 80
Leu Thr Phe Trp Glu Ala Ser Gln Leu Tyr Leu Leu Phe Leu Ser Leu
85 90 95
Thr Leu Ala Thr Val Asn Ala Arg Trp Leu Glu Pro Arg Thr Thr Ala
100 105 110

25 Ala Met Trp Ala Leu Gln Thr Val Glu Lys Glu Arg Gly Leu Gly Gly
115 120 125
Glu Val Pro Gly Ser His Gln Gly Pro Asp Pro Tyr Arg Gln Leu Arg
130 135 140
Glu Lys Asp Pro Lys Tyr Ser Ala Leu Arg Gln Asn Phe Phe Arg Tyr
30 145 150 155 160
His Gly Leu Ser Ser Leu Cys Asn Leu Gly Cys Val Leu Ser Asn Gly
165 170 175
Leu Cys Leu Ala Gly Leu Ala Leu Glu Ile Arg Ser Leu
180 185

35

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<210> 36

<211> 363

<212> PRT

<213> Homo sapiens

5

<400> 36

Met Val Asp Ser Leu Leu Ala Val Thr Leu Ala Gly Asn Leu Gly Leu

1

5

10

15

Thr Phe Leu Arg Gly Ser Gln Thr Gln Ser His Pro Asp Leu Gly Thr

10

20

25

30

Glu Gly Cys Trp Asp Gln Leu Ser Ala Pro Arg Thr Phe Thr Leu Leu

35

40

45

Asp Pro Lys Ala Ser Leu Leu Thr Lys Ala Phe Leu Asn Gly Ala Leu

50

55

60

15

Asp Gly Val Ile Leu Gly Asp Tyr Leu Ser Arg Thr Pro Glu Pro Arg

65

70

75

80

Pro Ser Leu Ser His Leu Leu Ser Gln Tyr Tyr Gly Ala Gly Val Ala

85

90

95

Arg Asp Pro Gly Phe Arg Ser Asn Phe Arg Arg Gln Asn Gly Ala Ala

20

100

105

110

Leu Thr Ser Ala Ser Ile Leu Ala Gln Gln Val Trp Gly Thr Leu Val

115

120

125

Leu Leu Gln Arg Leu Glu Pro Val His Leu Gln Leu Gln Cys Met Ser

130

135

140

25

Gln Glu Gln Leu Ala Gln Val Ala Ala Asn Ala Thr Lys Glu Phe Thr

145

150

155

160

Glu Ala Phe Leu Gly Cys Pro Ala Ile His Pro Arg Cys Arg Trp Gly

165

170

175

Ala Ala Pro Tyr Arg Gly Arg Pro Lys Leu Leu Gln Leu Pro Leu Gly

30

180

185

190

Phe Leu Tyr Val His His Thr Tyr Val Pro Ala Pro Pro Cys Thr Asp

195

200

205

Phe Thr Arg Cys Ala Ala Asn Met Arg Ser Met Gln Arg Tyr His Gln

210

215

220

35

Asp Thr Gln Gly Trp Gly Asp Ile Gly Tyr Ser Phe Val Val Gly Ser

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225 230 235 240
 Asp Gly Tyr Val Tyr Glu Gly Arg Gly Trp His Trp Val Gly Ala His
 245 250 255
 Thr Leu Gly His Asn Ser Arg Gly Phe Gly Val Ala Ile Val Gly Asn
 5 260 265 270
 Tyr Thr Ala Ala Leu Pro Thr Glu Ala Ala Leu Arg Thr Val Arg Asp
 275 280 285
 Thr Leu Pro Ser Cys Ala Val Arg Ala Gly Leu Leu Arg Pro Asp Tyr
 290 295 300
 10 Ala Leu Leu Gly His Arg Gln Leu Val Arg Thr Asp Cys Pro Gly Asp
 305 310 315 320
 Ala Leu Phe Asp Leu Leu Arg Thr Trp Pro His Phe Thr Ala Thr Val
 325 330 335
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 15 340 345 350
 Pro Pro Arg Thr Leu Pro Ala Thr Asp Leu Gln
 355 360

 <210> 37
 20 <211> 249
 <212> PRT
 <213> Homo sapiens

 <400> 37
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 20 25 30
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 30 35 40 45
 Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala Glu Gln Leu Gln
 50 55 60
 Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro Val Ile Ile Glu
 65 70 75 80
 35 Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Ala Phe Ser Val Asn Gln

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	85	90	95
	Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val Ala Asn Lys Ile		
	100	105	110
5	Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu Asn Ala Leu Asn		
	115	120	125
	Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile Lys Val Gln Val		
	130	135	140
	Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala Met Thr Glu Gly		
	145	150	155
10	Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser Leu Tyr Asp Ser		
	165	170	175
	His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr Leu Phe Gln Asn		
	180	185	190
	Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala Val Gln Pro Thr		
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	Phe Thr Glu Gly Ser Leu Phe Phe Leu Leu His Gly Glu Cys Ala		
	210	215	220
	Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala Glu Val Lys Glu		
	225	230	235
20	Lys Val Val Thr Ile Ile Pro Lys Ile		
	245		
	<210> 38		
	<211> 98		
25	<212> PRT		
	<213> Homo sapiens		
	<400> 38		
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	20	25	30
	Phe Asn Val His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu		
	35	40	45
35	Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln		

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55
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Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly
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Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met
5 85 90 95
Val Arg

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10 <212> PRT
<213> Homo sapiens

<400> 39
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20 20 25 30
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35 40 45
20 Glu Glu Glu Leu Ala Arg Tyr Gly Gly Glu Glu Glu Asp Gln Pro Ile
50 55 60
Tyr Leu Ala Val Lys Gly Val Val Phe Asp Val Thr Ser Gly Lys Glu
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25 Phe Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Thr Gly Lys Asp Ser
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Thr Arg Gly Val Ala Lys Met Ser Leu Asp Pro Ala Asp Leu Thr His
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Asp Thr Thr Gly Leu Thr Ala Lys Glu Leu Glu Ala Leu Asp Glu Val
115 120 125
30 Phe Thr Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala
130 135 140
Arg Arg Ile Leu Asn Glu Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro
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Glu Asp Gln Pro His Phe Asp Ile Lys Asp Glu Phe
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<210> 40

<211> 120

<212> PRT

5 <213> Homo sapiens

<400> 40

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10

15

10 Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile Asp Leu

20

25

30

Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile Ala Leu

35

40

45

Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Gly Ser

15 50

55

60

Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg Ala Val

65

70

75

80

Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe Tyr His

85

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95

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110

Asp Asp Ile Pro Asp Phe Asp Asp

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120

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<211> 939

<212> DNA

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tgcaaggaaa tcaaagacga atgtctctagt gcatttgatg gcctgtattt tctccgact 180

gagaatgggt ttatctacca gacctctctg gacatgacct ctgggggtgg cggtgggacc 240

35 ctggtggcca gctgcatga gaatgacatg cgtgggaagt gcacgggtgg cgatcgctgg 300

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 aacacctttg gatctgcaga ggcggccacg agcgtgact acaagaaccc tggtactac 420
 gacatccag ccaaggacct gggcatctgg cactgtccc ataagtcgcc catgcagcac 480
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 tctttact cacctatgg ccagcgggaa ttcactgcgg gatttgtca gttcagggtta 720
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 actgagcacc actgcattgg tggaggagga tactttccag aggcagtc ccagcagtgt 840
 10 ggagattttt ctggttttga ttggagtgga tatggaaact atgttggtta cagcagcagc 900
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15 <212> DNA

<213> Homo sapiens

<400> 42

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 gagtaaccaag ttttagatgg agcaggatta gatattgatt tcatcttgc cttccagaa 240
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 25 tctcttgat taatcctgga taatatggga gaacaggcac aagaacaaga agattggaag 420
 aaatatatta ctggccagca tatattggat atgaaactgg aagacatcct ggaatccatc 480
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 gaagctcgtg atcgaaacat acaagaaagc aactttgata gactcaattt ctggtctatg- 600
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 30 tttgaagata agaggaaaag tagaact 687

<210> 43

<211> 1401

<212> DNA

35 <213> Homo sapiens

43/177

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	gtatctgtgt tggcaactgat accagaaacc acaacattga cagttggtgg aggggtgttt	180
	gcacttgtga cagcagtatg ctgtcttgcc gacggggccc ttatttacgg gaagcttctg	240
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	ccatccctca gccacttgct gagccagtae tatggggctg ggggtggccag agaccaggg	300
	ttcccgagca actccgacg gcagaacggt gctgctctga ctccagcctc catctggcc	360
	cagcaggtgt ggggaacctt tgcctctcta cagagggctg agccagttaca cctccagett	420
35	cagtgcata gccaagaaca gctggcccag gtggctgcca atgtaccaa ggaattcaat	480

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 ggccatttag ctgtgcagcc tacttttact gaaggttcat tgtttttcct gttacatgga 660
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<211> 294

35 <212> DNA

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<213> Homo sapiens

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	attgaggacg	ttcccttcac	ggagaaagat	tttgagaatg	gccccagaa	catatacaac	180
	ctttacgagc	aagtcagcta	caactgtttc	atcgctgcag	gcctttacct	cctcctcgga	240
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10 <210> 49

<211> 516

<212> DNA

<213> Homo sapiens

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	gggccccag	tgcggctttt	caccgaggag	gagctggccc	gctatggcgg	ggaggaggaa	180
	gacagccca	tctacttggc	agtgaaggga	gtggtgtttg	atgtcacctc	cggaaaggag	240
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	gccaaagtgt	ccttggtatc	tgacagacct	acctatgaca	ctacgggtct	cacggccaag	360
	gaactggagg	ccctggatga	ggtcttcacc	aaagtgtaca	aagccaaata	ccccatctgc	420
	ggctacactg	cccggagaat	tctcaatgag	gatggcagcc	ctaactcgga	cttcaagcct	480
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25

<210> 50

<211> 360

<212> DNA

<213> Homo sapiens

30

<400> 50

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ccagtgtgta tcattggcat tctgggtgtc ctaccggat ttaccacct ggcgacgct 300
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 Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser
 20 20 25 30
 tgc tct cca tct ctg ccc aga agc tgc aag gaa atc aaa gac gaa tgt 145
 20 Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys
 35 40 45
 cct agt gca ttt gat ggc ctg tat ttt ctc cgc act gag aat ggt gtt 193
 Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val
 50 55 60
 25 atc tac cag acc ttc tgt gac atg acc tct ggg ggt ggc ggc tgg acc 241
 Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Gly Trp Thr
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 ctg gtg gcc agc gtg cat gag aat gac atg cgt ggg aag tgc acg gtg 289
 Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val
 30 85 90 95
 ggc gat cgc tgg tcc agt cag cag ggc agc aaa gca gac tac cca gag 337
 Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Glu
 100 105 110
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 35 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala

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	Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala			
	130	135	140	
5	aag gac ctg ggc atc tgg cac gtg ccc aat aag tcc ccc atg cag cac			481
	Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His			
	145	150	155	160
	tgg aga aac agc tcc ctg ctg agg tac cgc acg gac act ggc ttc ctc			529
	Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu			
10		165	170	175
	cag aca ctg gga cat aat ctg ttt ggc atc tac cag aaa tat cca gtg			577
	Gln Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val			
	180	185	190	
	aaa tat gga gaa gga aag tgt tgg act gac aac ggc ccg gtg atc cct			625
15	Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro			
	195	200	205	
	gtg gtc tat gat ttt ggc gac gcc cag aaa aca gca tct tat tac tca			673
	Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser			
	210	215	220	
20	ccc tat ggc cag cgg gaa ttc act gcg gga ttt gtt cag ttc agg gta			721
	Pro Tyr Gly Gln Arg Glu Phe Thr Ala Gly Phe Val Gln Phe Arg Val			
	225	230	235	240
	ttt aat aac gag aga gca gcc aac gcc ttg tgt gct gga atg agg gtc			769
	Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val			
25		245	250	255
	acc gga tgt aac act gag cac cac tgc att ggt gga gga gga tac ttt			817
	Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe			
	260	265	270	
	cca gag gcc agt ccc cag cag tgt gga gat ttt tct ggt ttt gat tgg			865
30	Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp			
	275	280	285	
	agt gga tat gga act cat gtt ggt tac agc agc agc cgt gag ata act			913
	Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr			
	290	295	300	
35	gag gca gct gtg ctt cta ttc tat cgt tgagagtttt gtgggaggga			960

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Glu Ala Ala Val Leu Leu Phe Tyr Arg

305

310

accacagacct ctctctcccaa ccatgagatc ccaaggatgg agaacaatt acccagtagc 1020

tagaatgtta atggcagaag agaaaacaat aatatcatatt gactc 1065

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<213> Homo sapiens

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<222> (177)...(866)

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tggagtttct taagaactcca gatttcctct tcaaccacga ggagtcacaga gaggaaacgc 120

ggagcggaga caacagtacc tgacgcctct ttcagccagg gatcgcccca gcaggg 176

atg ggc gac aag atc tgg ctg ccc ttc ccc gtg etc ctt ctg gcc gat 224

Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala

20

1	5	10	15	
ctg	cct	ccg	gtg	ctg
cct	ggg	gcg	gcc	ggc
ttc	aca	cct	tcc	etc

272

Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu

20

25

30

gat agc gac ttc acc ttt acc ctt ccc gcc ggc cag aag gag tgc ttc 320

25

Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe

35

40

45

tac cag ccc atg ccc ctg aag gcc tcg ctg gag atc gag tac caa gtt 368

Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val

50

55

60

30

tta gat gga gca gga tta gat att gat ttc cat ctt gcc tct cca gaa 416

Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu

65

70

75

80

ggc aaa acc tta gtt ttt gaa caa aga aaa tca gat gga gtt cac act 464

Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr

35

85

90

95

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	gta gag act gaa gtt ggt gat tac atg ttc tgc ttt gac aat aca ttc	512
	Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe	
	100 105 110	
	agc acc att tct gag aag gtg att ttc ttt gaa tta atc ctg gat aat	560
5	Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn	
	115 120 125	
	atg gga gaa cag gca caa gaa caa gaa gat tgg aag aaa tat att act	608
	Met Gly Glu Gln Ala Gln Glu Gln Glu Asp Trp Lys Lys Tyr Ile Thr	
	130 135 140	
10	ggc aca gat ata ttg gat atg aaa ctg gaa gac atc ctg gaa tcc atc	656
	Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile	
	145 150 155 160	
	aac agc atc aag tcc aga cta agc aaa agt ggg cac ata caa att ctg	704
	Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu	
15	165 170 175	
	ctt aga gca ttt gaa gct cgt gat cga aac ata caa gaa agc aac ttt	752
	Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe	
	180 185 190	
	gat aga gtc aat ttc tgg tct atg gtt aat tta gtg gtc atg gtg gtg	800
20	Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val	
	195 200 205	
	gtg tca gcc att caa gtt tat atg ctg aag agt ctg ttt gaa gat aag	848
	Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys	
	210 215 220	
25	agg aaa agt aga act taaaactcca aactagagta cgtaacattg aaaaatg	900
	Arg Lys Ser Arg Thr	
	225	
	aggcataaaa atgcataaaa ctgttacagt caagacc	937
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5	atg cgg ccc cag gag ctc ecc agg ctc ggg ttc cgg ttg ctg ctg ttg	103
	Met Arg Pro Gln Glu Leu Pro Arg Leu Ala Phe Pro Leu Leu Leu Leu	
	1 5 10 15	
	ctg ttg ctg ctg ctg ccg ccg ccg ccg tgc cct gcc cac agc gcc acg	151
	Leu Leu Leu Leu Leu Pro Pro Pro Pro Cys Pro Ala His Ser Ala Thr	
10	20 25 30	
	cgc ttc gac ccc acc tgg gag tcc ctg gac gcc cgc cag ctg ccc ggg	199
	Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala	
	35 40 45	
	tgg ttt gac cag gcc aag ttc ggc atc ttc atc cac tgg gga gtg ttt	247
15	Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe	
	50 55 60	
	tcc gtg ccc agc ttc ggt agc gag tgg ttc tgg tgg tat tgg caa aag	295
	Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Gln Lys	
	65 70 75 80	
20	gaa aag ata ccg aag tat gtg gaa ttt atg aaa gat aat tac cct cct	343
	Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro	
	85 90 95	
	agt ttc aaa tat gaa gat ttt gga cca cta ttt aca gca aaa ttt ttt	391
	Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe	
25	100 105 110	
	aat gcc aac cag tgg gca gat att ttt cag gcc tct ggt gcc aaa tac	439
	Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr	
	115 120 125	
	att gtc tta act tcc aaa cat cat gaa ggc ttt acc ttg tgg ggg toa	487
30	Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser	
	130 135 140	
	gaa tat tcg tgg aac tgg aat gcc ata gat gag ggg ccc aag agg gac	535
	Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp	
	145 150 155 160	
35	att gtc aag gaa ctt gag gta gcc att agg aac aga act gac ctg cgt	583

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	Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg	
	165 170 175	
	ttt gga ctg tac tat tcc ctt ttt gaa tgg ttt cat ccg ctc ttc ctt	631
	Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu	
5	180 185 190	
	gag gat gaa tcc agt tca ttc cat aag cgg caa ttt cca gtt tct aag	679
	Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys	
	195 200 205	
	aca ttg cca gag ctc tat gag tta gtg aac aac tat cag cct gag gtt	727
10	Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val	
	210 215 220	
	ctg tgg tgg gat ggt gac gga gga gca ccg gat caa tac tgg aac agc	775
	Leu Trp Ser Asp Gly Asp Gly Gly Ala Pro Asp Gln Tyr Trp Asn Ser	
	225 230 235 240	
15	aca ggc ttc ttg gcc tgg tta tat aat gaa agc cca gtt cgg ggc aca	823
	Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr	
	245 250 255	
	gta gtc acc aat gat cgt tgg gga gct ggt agc atc tgt aag cat ggt	871
	Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly	
20	260 265 270	
	ggc ttc tat acc tgc agt gat cgt tat aac cca gga cat ctt ttg cca	919
	Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro	
	275 280 285	
	cat aaa tgg gaa aac tgc atg aca ata gac aaa ctg tcc tgg ggc tat	967
25	His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr	
	290 295 300	
	agg agg gaa gct gga atc tct gac tat ctt aca att gaa gaa ttg gtg	1015
	Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val	
	305 310 315 320	
30	aag caa ctt gta gag aca gtt tca tgt gga gga aat ctt ttg atg aat	1063
	Lys Gln Leu Val Glu Thr Val Ser Cys Gly Gly Asn Leu Leu Met Asn	
	325 330 335	
	att ggg ccc aca cta gat ggc acc att tct gta gtt ttt gag gag cga	1111
	Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg	
35	340 345 350	

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ctg agg caa atg ggg tcc tgg cta aaa gtc aat gga gaa gct att tat 1159
 Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr
 355 360 365
 gaa acc cat acc tgg cga tcc cag aat gac act gtc acc cca gat gtg 1207
 5 Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val
 370 375 380
 tgg tac aca tcc aag cct aaa gaa aaa tta gtc tat gcc att ttt ctt 1255
 Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu
 385 390 395 400
 10 aza tgg ccc aca tca gga cag ctg ttc ctt ggc cat ccc aaa gct att 1303
 Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile
 405 410 415
 ctg ggg gca aca gag gtg aaa cta ctg ggc cat gga cag cca ctt aac 1351
 Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn
 15 420 425 430
 tgg att tct ttg gag caa aat ggc att atg gta gaa ctg cca cag cta 1399
 Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu
 435 440 445
 acc att cat cag atg ccg tgt aaa tgg ggc tgg gct cta gcc ctg act 1447
 20 Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr
 450 455 460
 aat gtg atc taaagtgcag cagagtggct gatgctgcaa gttatgtcta aggc 1500
 Asn Val Ile
 465
 25 taggaactat caggtgtota taattgtagc acatggagaa agcaaatgta aaactggata 1560
 agaaaaattat ttggcagtt cagccctttc cctttttccc actaaatttt ttcttaaat 1620
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 cagccagctg agaagagttg agggaaagtg ctgctgctgg gttgcagac gcg atg 116

5

Met

1

gat aac gtg cag ccg aaa ata aaa cat cgc ccc ttc tgc ttc agt gtg 164
 Asp Asn Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser Val

5

10

15

10

aaa ggc cac gtg aag atg ctg cgg ctg gat att atc aac tca ctg gta 212
 Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu Val

20

25

30

aca aca gta ttc atg ctc atc gta tct gtg ttg gca ctg ata cca gaa 260
 Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro Glu

15

35

40

45

acc aca aca ttg aca gtt ggt gga ggg gtg ttt gca ctt gtg aca gca 308
 Thr Thr Thr Leu Thr Val Gly Gly Gly Val Phe Ala Leu Val Thr Ala

50

55

60

65

gta tgc tgt ctt gcc gac ggg gcc ctt att tac cgg aag ctt ctg ttc 356
 Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu Phe

20

70

75

80

aat ccc agc ggt cct tac cag caa aag cct gtg cat gaa aaa aaa gaa 404
 Asn Pro Ser Gly Pro Tyr Gln Gln Lys Pro Val His Glu Lys Lys Glu

85

90

95

25

gtt ttg taattttata ttacttttta gtttgatact aagtattaaa 450
 Val Leu

catatttotg tatttett

467

30

<210> 55

<211> 875

<212> DNA

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WO 00/05367

PCT/IP99/03929

55/177

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	gggtgctgcg gattgaggtc ccggttcccta acgaatctct gctggattgg ccgtaacctt	180
	gtccccgagc gggtccacag ggtctgaagg ccacgcataa ggcgaaggta aagttctgag	240
	ccaccgggtg cctccttccc aggaactgcaa g atg gag gaa ggc ggg aac cta	292
	Met Glu Glu Gly Gly Asn Leu	
10	1 5	
	gga ggc ctg att aag atg gtc cat cta ctg gtc ttg tca ggt gcc tgg	340
	Gly Gly Leu Ile Lys Met Val His Leu Leu Val Leu Ser Gly Ala Trp	
	10 15 20	
	ggc atg caa atg tgg gtg acc ttc gtc tca ggc ttc ctg ctt ttc cga	388
15	Gly Met Gln Met Trp Val Thr Phe Val Ser Gly Phe Leu Leu Phe Arg	
	25 30 35	
	agc ctt ccc cga cat acc ttc gga cta gtg cag agc aaa ctc ttc ccc	436
	Ser Leu Pro Arg His Thr Phe Gly Leu Val Gln Ser Lys Leu Phe Pro	
	40 45 50 55	
20	ttc tac ttc cac atc tcc atg ggc tgt gcc ttc atc aac ctc tgc atc	484
	Phe Tyr Phe His Ile Ser Met Gly Cys Ala Phe Ile Asn Leu Cys Ile	
	60 65 70	
	ttg gct tca cag cat gct tgg gct cag ctc aca ttc tgg gag gcc agc	532
	Leu Ala Ser Gln His Ala Trp Ala Gln Leu Thr Phe Trp Glu Ala Ser	
25	75 80 85	
	cag ctt tac ctg ctg ttc ctg agc ctt acg ctg gcc act gtc aac gcc	580
	Gln Leu Tyr Leu Leu Phe Leu Ser Leu Thr Leu Ala Thr Val Asn Ala	
	90 95 100	
	cgc tgg ctg gaa ccc cgc acc aca gct gcc atg tgg gcc ctg caa acc	628
30	Arg Trp Leu Glu Pro Arg Thr Thr Ala Ala Met Trp Ala Leu Gln Thr	
	105 110 115	
	gtg gag aag gag cga ggc ctg ggt ggg gag gta cca ggc agc cac cag	676
	Val Glu Lys Glu Arg Gly Leu Gly Gly Glu Val Pro Gly Ser His Gln	
	120 125 130 135	
35	ggt ccc gat ccc tac cgc cag ctg cga gag aag gac ccc aag tac agt	724

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Gly Pro Asp Pro Tyr Arg Gln Leu Arg Glu Lys Asp Pro Lys Tyr Ser
 140 145 150
 gct ctc cgc cag aat ttc ttc cgc tac cat ggg ctg tcc tct ctt tgc 772
 Ala Leu Arg Gln Asn Phe Phe Arg Tyr His Gly Leu Ser Ser Leu Cys
 5 155 160 165
 aat ctg ggc tgc gtc ctg agc aat ggg ctc tgt ctc gct ggc ctt gcc 820
 Asn Leu Gly Cys Val Leu Ser Asn Gly Leu Cys Leu Ala Gly Leu Ala
 170 175 180
 ctg gaa ata agg agc ctc tagcatgggc cctgcattgct aataaatgct tcttcag 875
 10 Leu Glu Ile Arg Ser Leu
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 cagatgccaa agccaagtcc ccaccgacc atg gtg gac agc ctc ctg gca gtc 173
 25 Met Val Asp Ser Leu Leu Ala Val
 1 5
 acc ctg gct gga aac ctg ggc ctg acc ttc ctc cga ggt tcc cag acc 221
 Thr Leu Ala Gly Asn Leu Gly Leu Thr Phe Leu Arg Gly Ser Gln Thr
 10 15 20
 30 cag agc cat cca gac ctg gga act gag ggc tgc tgg gac cag ctc tct 269
 Gln Ser His Pro Asp Leu Gly Thr Glu Gly Cys Trp Asp Gln Leu Ser
 25 30 35 40
 gcc cct egg acc ttt acg ctt ttg gac ccc aag gca tct ctg tta acc 317
 Ala Pro Arg Thr Phe Thr Leu Leu Asp Pro Lys Ala Ser Leu Leu Thr
 35 45 50 55

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	Lys Ala Phe Leu Asn Gly Ala Leu Asp Gly Val Ile Leu Gly Asp Tyr	
	60 65 70	
	ctg agc cgg act cct gag ccc cgg cca tcc ctc agc cac ttg ctg agc	413
5	Leu Ser Arg Thr Pro Glu Pro Arg Pro Ser Leu Ser His Leu Leu Ser	
	75 80 85	
	cag tac tat ggg gct ggg gtg gcc aga gac cca ggg ttc cgc agc aac	461
	Gln Tyr Tyr Gly Ala Gly Val Ala Arg Asp Pro Gly Phe Arg Ser Asn	
	90 95 100	
10	ttc cga cgg cag aac ggt gct gct ctg act tca gcc tcc atc ctg gcc	509
	Phe Arg Arg Gln Asn Gly Ala Ala Leu Thr Ser Ala Ser Ile Leu Ala	
	105 110 115 120	
	cag cag gtg tgg gga acc ctt gtc ctt cta cag agg ctg gag cca gta	557
	Gln Gln Val Trp Gly Thr Leu Val Leu Leu Gln Arg Leu Glu Pro Val	
15	125 130 135	
	cac ctc cag ctt cag tgc atg agc caa gaa cag ctg gcc cag gtg gct	605
	His Leu Gln Leu Gln Cys Met Ser Gln Glu Gln Leu Ala Gln Val Ala	
	140 145 150	
	gcc aat gct acc aag gaa ttc act gag gcc ttc ctg gga tgc ccg gcc	653
20	Ala Asn Ala Thr Lys Glu Phe Thr Glu Ala Phe Leu Gly Cys Pro Ala	
	155 160 165	
	atc cac ccc cgc tgc cgc tgg gga gcg gcg cct tat cgg ggc cgc ccg	701
	Ile His Pro Arg Cys Arg Trp Gly Ala Ala Pro Tyr Arg Gly Arg Pro	
	170 175 180	
25	aag ctg ctg cag ctg ccg ctg gga ttc ttg tac gtg cat cac acc tac	749
	Lys Leu Leu Gln Leu Pro Leu Gly Phe Leu Tyr Val His His Thr Tyr	
	185 190 195 200	
	gtg cct gca cca ccc tgc acg gac ttc acg cgc tgc gca gcc aac atg	797
	Val Pro Ala Pro Pro Cys Thr Asp Phe Thr Arg Cys Ala Ala Asn Met	
30	205 210 215	
	cgc tcc atg cag cgc tac cac cag gac acg caa ggc tgg gga gac atc	845
	Arg Ser Met Gln Arg Tyr His Gln Asp Thr Gln Gly Trp Gly Asp Ile	
	220 225 230	
	ggc tac agt ttc gtg gtg gcc tgc gac gcc tac gtg tac gag gga cgc	893
35	Gly Tyr Ser Phe Val Val Gly Ser Asp Gly Tyr Val Tyr Glu Gly Arg	

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	235	240	245	
	ggc tgg cac tgg gtg ggc gcc cac acg ctc ggc cac aac tcc cgg ggc			941
	Gly Trp His Trp Val Gly Ala His Thr Leu Gly His Asn Ser Arg Gly			
	250	255	260	
5	ttc ggc gtg gcc ata gtg ggc aac tac acc gcg gcg ctg ccc acc gag			989
	Phe Gly Val Ala Ile Val Gly Asn Tyr Thr Ala Ala Leu Pro Thr Glu			
	265	270	275	280
	gcc gct ctg cgc acg gtg cgc gac acg ctc ccg agt tgt gcg gtg cgc			1037
	Ala Ala Leu Arg Thr Val Arg Asp Thr Leu Pro Ser Cys Ala Val Arg			
10		285	290	295
	gcc ggc ctc ctg cgg cca gac tac gcg ctg ctg ggc cac cgc cag ctg			1085
	Ala Gly Leu Leu Arg Pro Asp Tyr Ala Leu Leu Gly His Arg Gln Leu			
	300	305	310	
	gtg cgc acc gac tgc ccc ggc gac gcg ctc ttc gac ctg ctg cgc acc			1133
15	Val Arg Thr Asp Cys Pro Gly Asp Ala Leu Phe Asp Leu Leu Arg Thr			
	315	320	325	
	tgg ccg cac ttc acc gcg act gtt aag cca aga cct gcc agg agt gtc			1181
	Trp Pro His Phe Thr Ala Thr Val Lys Pro Arg Pro Ala Arg Ser Val			
	330	335	340	
20	tct aag aga tcc agg agg gag cca ccc cca agg acc ctg cca gcc aca			1229
	Ser Lys Arg Ser Arg Arg Glu Pro Pro Pro Arg Thr Leu Pro Ala Thr			
	345	350	355	360
	gac ctc caa taaagacagc atggaaac			1256
	Asp Leu Gln			
25	<210> 57			
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	gctggagacc	tcgcgctgg	ccccgcgag	cctcctgcc	tgcccgcg	ctgcgctet	120
	gcgcgcgcgc	cagc	atg	ggt	ggc	ccc	170
		Met	Gly	Gly	Pro	Arg	
		1		5		10	
5	ggc	ctg	ctg	ctc	ggc	gcg	218
	Gly	Leu	Leu	Leu	Gly	Ala	
		15		20		25	
	cgg	ggt	cgg	cgg	ggc	gac	266
	Arg	Gly	Arg	Arg	Gly	Asp	
10		30		35		40	
	tcc	gca	gaa	gac	tta	act	314
	Ser	Ala	Glu	Asp	Leu	Thr	
		45		50		55	
	gaa	caa	ctt	cag	aaa	ctc	362
15	Glu	Gln	Leu	Gln	Lys	Leu	
			65		70		
	gta	att	att	gaa	aga	gct	410
	Val	Ile	Ile	Glu	Arg	Ala	
			80		85		
20	tca	gtt	aac	caa	gct	att	458
	Ser	Val	Asn	Gln	Ala	Ile	
			95		100		
	gca	aac	aaa	atc	aac	cat	506
	Ala	Asn	Lys	Ile	Asn	His	
25		110		115		120	
	aat	gca	cta	aat	aac	ctg	554
	Asn	Ala	Leu	Asn	Asn	Leu	
		125		130		135	
	aag	gtg	caa	gtt	ttg	aaa	602
30	Lys	Val	Gln	Val	Leu	Lys	
			145		150		
	atg	aca	gaa	gga	ctt	ctc	650
	Met	Thr	Glu	Gly	Leu	Leu	
			160		165		
35	ctt	tat	gac	agc	cac	gta	698

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Leu Tyr Asp Ser His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr
 175 180 185
 cta ttt cag aat ata aag aac tgc ctc aaa ata gaa ggc cat tta gct 746
 Leu Phe Gln Asn Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala
 5 190 195 200
 gtg cag cct act ttc act gaa ggt tca ttg ttt ttc ctg tta cat gga 794
 Val Gln Pro Thr Phe Thr Glu Gly Ser Leu Phe Phe Leu Leu His Gly
 205 210 215 220
 gaa gaa tgt gcc cag aaa ata aga gct tta gtt gat cac cat gat gca 842
 10 Glu Glu Cys Ala Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala
 225 230 235
 gag gtg aag gaa aag gtt gta aca ata ata ccc aaa atc tga 884
 Glu Val Lys Glu Lys Val Val Thr Ile Ile Pro Lys Ile
 240 245
 15
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 20 <220>
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 25 gctttccgag cccgcttgca cctcggcgat ccccgactcc cttcttt atg gcg tgc 56
 Met Ala Ser
 1
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 Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile Val Leu Ser
 30 5 10 15
 gcc tgg gga gtg atc atg ttg ata atg ctc gga ata ttt ttc aat gtc 152
 Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe Phe Asn Val
 20 25 30 35
 cat tcc gct gtg ttg att gag gac gtt ccc ttc acg gag aaa gat ttt 200
 35 His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu Lys Asp Phe

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	40	45	50	
	gag aat ggc ccc cag aac ata tac aac ctt tac gag caa gtc agc tac			248
	Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln Val Ser Tyr			
	55	60	65	
5	aac tgt ttc atc gct gca ggc ctt tac ctc ctc ctc gga ggc ttc tct			296
	Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly Gly Phe Ser			
	70	75	80	
	ttc tgc caa gtt cgg ctc aat aag cgc aag gaa tac atg gtg cgc			341
	Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met Val Arg			
10	85	90	95	
	tagggcccc ggcgcgttcc cccgctccag cccctcctct atttaaagac tccctgcacc			400
	gtgtcaccaca ggtcgcgtcc cacccttgcc ggccgcctct gtgggactgg gtttcccggy			460
	cgagagactg aatccctctt cccatctctg gcacccggcc cccgtggaga gggctgaggc			520
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	Met Val Gly Pro Ala Pro Arg Arg Arg			
	1	5		
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30	Leu Arg Pro Leu Ala Ala Leu Ala Leu Val Leu Ala Leu Ala Pro Gly			
	10	15	20	25
	ctg ccc aca gcc cgg gcc ggg cag aca ccg cgc cct gcc gag cgg ggg			147
	Leu Pro Thr Ala Arg Ala Gly Gln Thr Pro Arg Pro Ala Glu Arg Gly			
	30	35	40	
35	ccc cca gtg cgg ctt ttc acc gag gag gag ctg gcc cgc tat ggc ggg			195

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Pro Pro Val Arg Leu Phe Thr Glu Glu Glu Leu Ala Arg Tyr Gly Gly
 45 50 55
 gag gag-gaa gat cag ccc atc tac ttg gca gtg aag gga gtg ttg ttt 243
 Glu Glu Glu Asp Gln Pro Ile Tyr Leu Ala Val Lys Gly Val Val Phe
 5 60 65 70
 gat gtc acc tcc gga aag gag ttt tat gga cga gga gcc ccc tac aat 291
 Asp Val Thr Ser Gly Lys Glu Phe Tyr Gly Arg Gly Ala Pro Tyr Asn
 75 80 85
 gcc ttg acg ggg aag gac tcc act aga ggg gta gcc aag atg tcc ttg 339
 10 Ala Leu Thr Gly Lys Asp Ser Thr Arg Gly Val Ala Lys Met Ser Leu
 90 95 100 105
 gat cct goa gac ctc acc cat gac act acg ggt ctc acg gcc aag gaa 387
 Asp Pro Ala Asp Leu Thr His Asp Thr Thr Gly Leu Thr Ala Lys Glu
 110 115 120
 15 ctg gag gcc ctg gat gag gtc ttc acc aaa gtg tac aaa gcc aaa tac 435
 Leu Glu Ala Leu Asp Glu Val Phe Thr Lys Val Tyr Lys Ala Lys Tyr
 125 130 135
 ccc atc gtc ggc tac act gcc cgg aga att ctc aat gag gat ggc agc 483
 Pro Ile Val Gly Tyr Thr Ala Arg Arg Ile Leu Asn Glu Asp Gly Ser
 20 140 145 150
 cct aac ctg gac ttc aag cct gaa gac cag ccc cat ttt gac atc aag 531
 Pro Asn Leu Asp Phe Lys Pro Glu Asp Gln Pro His Phe Asp Ile Lys
 155 160 165
 gat gag ttc tgatgttccc cctgcaggag caggtttcttg ggagcgtgag 580
 25 Asp Glu Phe
 170
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30 <210> 60
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 35 <221> CDS

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<22> (127)...(489)

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	cgtgtt atg atg ccg tcc cgt acc aac ctg gct act gga atc ccc agt	168
	Met Met Pro Ser Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser	
	1 5 10	
	agt aaa gtg aaa tat tca agg ctc tcc agc aca gac gat ggc tac att	216
10	Ser Lys Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile	
	15 20 25 30	
	gac ctt cag ttt aag aaa acc cct cct aag atc cct tat aag gcc atc	264
	Asp Leu Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile	
	35 40 45	
15	gca ctt gcc act gtg ctg ttt ttg att ggc gcc ttt ctc att att ata	312
	Ala Leu Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile	
	50 55 60	
	ggc tcc ctc ctg ctg tca ggc tac atc agc aaa ggg ggg gca gac cgg	360
	Gly Ser Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg	
20	65 70 75	
	gcc gtt cca gtg ctg atc att ggc att ctg gtg ttc cta ccc gga ttt	408
	Ala Val Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe	
	80 85 90	
	tac cac ctg cgc atc gct tac tat gca tcc aaa ggc tac cgt ggt tac	456
25	Tyr His Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr	
	95 100 105 110	
	tcc tat gat gac att cca gac ttt gat gac tagcaccac ccca	500
	Ser Tyr Asp Asp Ile Pro Asp Phe Asp Asp	
	115 120	
30	tagctgagga ggagtcacag tggaactgtc ccagctttaa gatattctagc agaaactata	560
	gctgaggact aaggaattct gcagcttgca gatgtttaag aaaataatgg ccagattttt	620
	tgggtccttc ccaaagatgt taagtgaacc tacagtttagc taattaggac aagctctatt	680
	tttcatccct gggccctgac aagtttttcc acaggaatat gtatcatgga agaatagagg	740
	ttattctgta atggaaaaagt gttgcctgcc accaccctct gtagagctga gcatttcttt	800
35	taaatagctt tcatgcccac ttgtttcttg tagcaaatgg aacaatgtgg tatggcataat	860

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ttcttattat taagtagttt attttaaaaa tatctgagta tattatcctg tacacttacc 920
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aatatttttt ttacttgott tcttactgac agcaaccagg aattttttta tctgcagag 1040
caagttttca aaatgtaaat acttctcttg ttttaacagtc cttggaccat tctgatccag 1100
5 ttcaccagta ggttgacag catataattt gcatcatttt gtcccttgta aatcaagatg 1160
ttctgcagat tattccttta acggccggac ttttggtgtg ttccctaatga aacatgtagt 1220
ggttattatt tagagtatt agccgtattg ctagcactt gtagtatgtc atcattctgc 1280
tcatgattcc aaggatcagc ctggatgcct agaggactag atcaccttag ttgatttota 1340
tttttagct tgcaaaaagt gacttatatt ccaagaagaat taaaatgttg aaatccaat 1400
10 cctagaaata aaatgagtta acttc 1425

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<211> 307

<212> PRT

15 <213> Homo sapiens

<400> 61

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    20             25             30
Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln Leu Pro
    35             40             45
25 Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe Ile Ser
    50             55             60
Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr Pro Asn
    65             70             75             80
Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Gln Lys Glu Phe Ile Thr --
    85             90             95
30 Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr Cys Phe
    100            105            110
Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr Asn Asn
    115            120            125
Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln Thr Glu
100            130            135            140

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Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu Gly Ser
 145 150 155 160
 Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly Ala Gly
 165 170 175
 5 Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu Ser Gly
 180 185 190
 Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn Leu Ile
 195 200 205
 Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly Asp Asp
 10 210 215 220
 Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys Leu Tyr
 225 230 235 240
 Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val Lys Ser
 245 250 255
 15 Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu Tyr Glu
 260 265 270
 Leu Arg Asn Leu Trp Gln Leu Phe Phe His Val Thr Val Gly Ala Phe
 275 280 285
 Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala Pro Asp
 20 290 295 300
 Tyr Asp Val
 305

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 25 <211> 183
 <212> PRT
 <213> Homo sapiens

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 1 5 10 15
 Trp Ala Ile Glu Leu Ser Gly Pro Gly Gly Gly Ser Arg Gly Arg Ser
 20 25 30
 Asp Arg Gly Ser Gly Gln Gly Asp Ser Leu Tyr Pro Val Gly Tyr Leu
 35 35 40 45

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Asp Lys Gln Val Pro Asp Thr Ser Val Gln Glu Thr Asp Arg Ile Leu
 50 55 60
 Val Glu Lys Arg Cys Trp Asp Ile Ala Leu Gly Pro Leu Lys Gln Ile
 65 70 75 80
 5 Pro Met Asn Leu Phe Ile Met Tyr Met Ala Gly Asn Thr Ile Ser Ile
 85 90 95
 Phe Pro Thr Met Met Val Cys Met Met Ala Trp Arg Pro Ile Gln Ala
 100 105 110
 Leu Met Ala Ile Ser Ala Thr Phe Lys Met Leu Glu Ser Ser Ser Gln
 10 115 120 125
 Lys Phe Leu Gln Gly Leu Val Tyr Leu Ile Gly Asn Leu Met Gly Leu
 130 135 140
 Ala Leu Ala Val Tyr Lys Cys Gln Ser Met Gly Leu Leu Pro Thr His
 145 150 155 160
 15 Ala Ser Asp Trp Leu Ala Phe Ile Glu Pro Pro Glu Arg Met Glu Phe
 165 170 175
 Ser Gly Gly Gly Leu Leu Leu
 180
 20 <210> 63
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 <212> PRT
 <213> Homo sapiens
 25 <400> 63
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 20 25 30
 30 Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro Pro Leu Arg Glu
 35 40 45
 Glu Ile Met Ala Asn Asn Phe Ser Leu Glu Ser His Asn Ile Ser Leu
 50 55 60
 Thr Glu His Ser Ser Met Pro Val Glu Lys Asn Ile Thr Leu Glu Arg
 35 65 70 75 80

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Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr Ser Gly Asp Leu
 85 90 95
 Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Glu Gln Leu Glu Asn
 100 105 110
 5 Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr Thr Gln Tyr Arg
 115 120 125
 Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr Ser Cys Phe Phe
 130 135 140
 Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe Lys Val Pro Glu
 10 145 150 155 160
 Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val Gly Asp Ser Thr
 165 170 175
 Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu Asn Trp Thr Trp
 180 185 190
 15 Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly Val Gln Met Asn
 195 200 205
 Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr Lys Leu Lys Ile
 210 215 220
 Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp Cys Arg Ala Leu
 20 225 230 235 240
 Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu Val Val Leu Ser
 245 250 255
 Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val Ala Glu Val Ile
 260 265 270
 25 Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr Thr Gln Lys Lys
 275 280 285
 Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln Ile Glu Gln Leu
 290 295 300
 Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn Asn Val Pro Arg His Arg
 30 305 310 315 320
 Lys Asn Glu Ser Leu Gly Gln
 325

<210> 64

35 <211> 223

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<212> PRT

<213> Homo sapiens

<400> 64

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 Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Glu Glu
 20 25 30
 Phe His Phe Gln Thr Gly Gly Arg Asp Ser Cys Thr Met Arg Pro Ser
 10 35 40 45
 Ser Leu Gly Gln Gly Ala Gly Glu Val Trp Leu Arg Val Asp Cys Arg
 50 55 60
 Asn Thr Asp Gln Thr Tyr Trp Cys Glu Tyr Arg Gly Gln Pro Ser Met
 65 70 75 80
 15 Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala Leu
 85 90 95
 Gln Glu Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val Leu
 100 105 110
 Arg Pro Ser Val Cys Arg Glu Ala Gly Pro Gln Ala His Met Gln Gln
 20 115 120 125
 Val Thr Ser Ser Leu Lys Gly Ser Pro Glu Pro Asn Gln Gln Pro Glu
 130 135 140
 Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr Glu
 145 150 155 160
 25 Ala Thr Gln Leu Gly Lys Asp Ser Met Glu Glu Leu Gly Lys Ala Lys
 165 170 175
 Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg Pro
 180 185 190
 Gly Gly Asn Glu Glu Ala Lys Lys Lys Ala Trp Glu His Cys Trp Lys
 30 195 200 205
 Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly
 210 215 220

<210> 65

35 <211> 48

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<212> PRT

<213> Homo sapiens

<400> 65

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 Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys
 20 25 30
 10 Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser
 35 40 45

<210> 66

<211> 371

<212> PRT

15 <213> Homo sapiens

<400> 66

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 20 Thr Gly Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met
 20 25 30
 Ala Glu Gly Cys Gly Gly Ser Lys Glu His Ser Phe Gln His Pro Phe
 35 40 45
 25 Leu Gln Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala
 50 55 60
 Phe Tyr Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Ser Val
 65 70 75 80
 Asp Pro Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Pro Ala Leu
 85 90 95
 30 Cys Asp Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr
 100 105 110
 Ser Ala Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Ile Phe Thr
 115 120 125
 Gly Leu Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln
 130 135 140

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Trp Leu Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Val Gly Leu
 145 150 155 160
 Ala Asp Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val
 165 170 175
 5 Ile Thr Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile
 180 185 190
 Gln Met Val Leu Glu Glu Lys Phe Val Tyr Lys His Asn Val His Pro
 195 200 205
 10 Leu Arg Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser
 210 215 220
 Leu Leu Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly
 225 230 235 240
 Asn Pro Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val
 245 250 255
 15 Gly Gln Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser
 260 265 270
 Ile Ala Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser
 275 280 285
 Ala Thr Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp
 290 295 300
 20 Ala Leu Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile
 305 310 315 320
 Leu Gly Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu
 325 330 335
 25 His Arg Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu
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 Glu Ser Glu Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn
 355 360 365
 30 Asp Ala Ser
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 <212> PRT
 35 <213> Homo sapiens

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PCT/IP99/03929

71/177

<400> 67

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5 Leu Asn Ser Ile Tyr Gln Cys Pro Glu His Ser Gln Leu Thr Thr Leu
 20 25 30

Gly Val Asp Gly Lys Glu Phe Pro Glu Val His Leu Gly Gln Trp Tyr
 35 40 45

10 Phe Ile Ala Gly Ala Ala Pro Thr Lys Glu Glu Leu Ala Thr Phe Asp
 50 55 60

Pro Val Asp Asn Ile Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met
 65 70 75 80

Gln Leu His Leu Arg Ala Thr Ile Arg Met
 85 90

15

<210> 68

<211> 499

<212> PRT

<213> Homo sapiens

20

<400> 68

Met Val Asp Arg Gly Pro Leu Leu Thr Ser Ala Ile Ile Phe Tyr Leu
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25 Ala Ile Gly Ala Ala Ile Phe Glu Val Leu Glu Glu Pro His Trp Lys
 20 25 30

Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Lys Glu
 35 40 45

Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val
 50 55 60

30 Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe
 65 70 75 80

Asn Asn Trp Asn Trp Pro Asn Ala Met Ile Phe Ala Ala Thr Val Ile
 85 90 95

Thr Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg
 100 105 110

35

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Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr
 115 120 125
 Trp Ile Ser Ala Leu Gly Lys Phe Phe Gly Gly Arg Ala Lys Arg Leu
 130 135 140
 5 Gly Gln Phe Leu Thr Lys Arg Gly Val Ser Leu Arg Lys Ala Gln Ile
 145 150 155 160
 Thr Cys Thr Val Ile Phe Ile Val Trp Gly Val Leu Val His Leu Val
 165 170 175
 Ile Pro Pro Phe Val Phe Met Val Thr Glu Gly Trp Asn Tyr Ile Glu
 10 180 185 190
 Gly Leu Tyr Tyr Ser Phe Ile Thr Ile Ser Thr Ile Gly Phe Gly Asp
 195 200 205
 Phe Val Ala Gly Val Asn Pro Ser Ala Asn Tyr His Ala Leu Tyr Arg
 210 215 220
 15 Tyr Phe Val Glu Leu Trp Ile Tyr Leu Gly Leu Ala Trp Leu Ser Leu
 225 230 235 240
 Phe Val Asn Trp Trp Lys Val Ser Met Phe Val Glu Val His Lys Ala Ile
 245 250 255
 Lys Lys Arg Arg Arg Arg Arg Lys Glu Ser Phe Glu Ser Ser Pro His
 20 260 265 270
 Ser Arg Lys Ala Leu Gln Val Lys Gly Ser Thr Ala Ser Lys Asp Val
 275 280 285
 Asn Ile Phe Ser Phe Leu Ser Lys Lys Glu Glu Thr Tyr Asn Asp Leu
 290 295 300
 25 Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu
 305 310 315 320
 Thr Gly Pro Gly Pro Gly Leu Gly Pro Gln Gly Gly Gly Leu Pro Ala
 325 330 335
 Leu Pro Pro Ser Leu Val Pro Leu Val Tyr Ser Lys Asn Arg Val
 30 340 345 350
 Pro Thr Leu Glu Glu Val Ser Gln Thr Leu Arg Ser Lys Gly His Val
 355 360 365
 Ser Arg Ser Pro Asp Glu Glu Ala Val Ala Arg Ala Pro Glu Asp Ser
 370 375 380
 35 Ser Pro Ala Pro Glu Val Phe Met Asn Gln Leu Asp Arg Ile Ser Glu

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385 390 395 400
 Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln
 405 410 415
 Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu
 5 420 425 430
 Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser
 435 440 445
 Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe
 450 455 460
 10 Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser
 465 470 475 480
 Val Pro Tyr Glu Gln Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro
 485 490 495
 Lys Gly Thr
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 <210> 69
 <211> 106
 <212> PRT
 20 <213> Homo sapiens
 <400> 69
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 20 25 30
 Glu Gln Leu His Ser Met Arg Gln Ala Glu Leu Ala Gln Trp Gln Lys
 35 40 45
 Val Leu Pro Arg Arg Arg Thr Arg Asn Ile Val Thr Gly Leu Gly Ile
 30 50 55 60
 Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr Thr Phe Tyr Ser Ile Ser
 65 70 75 80
 Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp Glu Ala Lys Ala Ala Arg
 85 90 95
 35 Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser

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100

105

<210> 70

<211> 152

5 <212> PRT

<213> Homo sapiens

<400> 70

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 20 25 30
 Ala Gln Lys Gly Lys Ser Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile
 35 40 45
 15 Ser Leu Phe Leu Ile Ile Ser Met Cys Leu Leu Phe Leu Trp Lys Lys
 50 55 60
 Tyr Gln Pro Tyr Lys Val Ile Lys Gln Lys Leu Glu Gly Arg Pro Glu
 65 70 75 80
 Thr Glu Tyr Arg Lys Ala Gln Thr Phe Ser Gly His Glu Asp Ala Leu
 20 85 90 95
 Asp Asp Phe Gly Ile Tyr Glu Phe Val Ala Phe Pro Asp Val Ser Gly
 100 105 110
 Val Ser Arg Ile Pro Ser Arg Ser Val Pro Ala Ser Asp Cys Val Ser
 115 120 125
 25 Gly Gln Asp Leu His Ser Thr Val Tyr Glu Val Ile Gln His Ile Pro
 130 135 140
 Ala Gln Gln Gln Asp His Pro Glu
 145 150

30 <210> 71

<211> 921

<212> DNA

<213> Homo sapiens

35 <400> 71

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 tcgaggaaac ttgctcaact tcctgataga tgtacactga aaactggaca ttataacatt 180
 aattttatta gctctctggg agtgagctac atgatgtgt gcactgaaaa ttacccaaat 240
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<400> 72

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 atgggtgtga tgatggcctg gcgacccatt caggcaacta tggccattto agccacttct 360
 30 aagatgttag aaagtccaag ccagaagttt ctccagggtt tggctctatct cattgggaac 420
 ctgatggggt tggcattggc tgtttacaag tgccagtgca tgggactgtt acctacacat 480
 gcacgggatt ggtagccct cattgagccc cctgagagaa tggagttcag tggtgaggga 540
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35 <210> 73

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<211> 981

<212> DNA

<213> Homo sapiens

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 gattctcgca ctatcgctcc cagcagcttg gggcaagggtg ctggagaagt ctggcttcgc 180
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	gctgacctcc tgagcaagca cgacagtcag cacaagctca gcgaagtgat cacaggggac	540
	ctgttgatca tcatggccca gatcctggt gccatccaga tgggtgtaga ggagaaagtc	600
	gtctacaacc acaatgtgca cccactcggg gcagttggca ctgagggcct ctttggttt	660
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	aaccctcgtg ggacactgga ggatgcattg gacgccttct gccaggtggg ccagcagccg	780
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	tatggcaatg tggctcccaa gacccccgcc ggtcgcctct tctgtgtttt ctatggcttc	360
	ttcgggggtg cgtcttgctt gacgtggatc agtgccttgg gcaagttctt cgggggacgt	420
	gccaagagac tagggcagtt ccttaccacg agaggtgtga gtctgcggaa ggcgcagatc	480
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<211> 318

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<213> Homo sapiens

<400> 79

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 gggagctgtg cccactggca gaaggtccta ccacggcggc gaaccgggaa catcgtgacc 180
 ggcctaggca tcggggccct ggtgttggtt atttatggtt acacttcta ctcgatttcc 240
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<210> 80

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80/177

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 Met Ser Met Ile Leu Ser Ala Ser Val Ile Arg Val Arg Asp
 1 5 10
 gga ctg cca ctt tct gct tct act gat tat gaa caa agc aca gga atg 155
 25 Gly Leu Pro Leu Ser Ala Ser Thr Asp Tyr Glu Gln Ser Thr Gly Met
 15 20 25 30
 cag gag tgc aga aag tat ttt aaa atg ctt tcg agg aaa ctt gct caa 203
 Gln Glu Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln
 35 40 45
 30 ctt cct gat aga tgt aca ctg aaa act gga cat tat aac att aat ttt 251
 Leu Pro Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe
 50 55 60
 att agc tct ctg gga gtg agc tac atg atg ttg tgc act gaa aat tac 299
 Ile Ser Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr
 35 65 70 75

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	cca aat gtt ctc gcc ttc tct ttc ctg gat gag ctt cag aag gag ttc	347
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	att act act tat aac atg atg aag aca aat act gct gtc aga coa tac	395
5	Ile Thr Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr	
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	tgt ttc att gaa ttt gat aac ttc att cag agg acc aag cag cga tat	443
	Cys Phe Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr	
	115 120 125	
10	aat aat ccc agg tct ctt tca aca aag ata aat ctt tct gac atg cag	491
	Asn Asn Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln	
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	acg gaa atc aag ctg agg cct cct tat caa att tcc atg tgc gaa ctg	539
	Thr Glu Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu	
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	Gly Ser Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly	
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20	Ala Gly Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu	
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	tca ggg att gta gga ttt atc ctt agt ctt tta tgt gga gct ctg aat	683
	Ser Gly Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn	
	195 200 205	
25	tta att cga ggc ttt cat gct ata gaa agt ctc ctg cag agt gat ggt	731
	Leu Ile Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly	
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	gat gat ttt aat tac atc att gca ttt ttc ctt gga aca gca gcc tgc	779
	Asp Asp Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys	
30	225 230 235	
	ctt tac cag tgt tat tta ctt gtc tac tac acc ggc tgg cgg aat gtc	827
	Leu Tyr Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val	
	240 245 250	
	aaa tct ttt ttg act ttt ggc tta atc tgt cta tgc aac atg tat ctc	875
35	Lys Ser Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu	

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	Ala Phe Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala				
		290	295	300	
	ccc gat tat gat gtc tgacaccatc cttcagatct attgccttgg ctte				1020
	Pro Asp Tyr Asp Val				
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30	Met Thr Ala Gln Gly Gly Leu Val				
	1 5				
	gct aac cga ggc cgg cgc ttc aag tgg gcc att gag cta agc ggg cct				158
	Ala Asn Arg Gly Arg Arg Phe Lys Trp Ala Ile Glu Leu Ser Gly Pro				
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	45 50 55	
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	Val Gln Glu Thr Asp Arg Ile Leu Val Glu Lys Arg Cys Trp Asp Ile	
	60 65 70	
	gcc ttg ggt ccc ctc aaa cag att ccc atg aat ctc ttc atc atg tac	350
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	atg gca ggc aat act atc tcc atc ttc cct act atg atg gtg tgt atg	398
	Met Ala Gly Asn Thr Ile Ser Ile Phe Pro Thr Met Met Val Cys Met	
	90 95 100	
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	Met Ala Trp Arg Pro Ile Gln Ala Leu Met Ala Ile Ser Ala Thr Phe	
	105 110 115 120	
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	Lys Met Leu Glu Ser Ser Ser Gln Lys Phe Leu Gln Gly Leu Val Tyr	
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	Leu Ile Gly Asn Leu Met Gly Leu Ala Leu Ala Val Tyr Lys Cys Gln	
	140 145 150	
	tcc atg gga ctg tta cct aca cat gca tgc gat tgg tta gcc ttc att	590
25	Ser Met Gly Leu Leu Pro Thr His Ala Ser Asp Trp Leu Ala Phe Ile	
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	Glu Pro Pro Glu Arg Met Glu Phe Ser Gly Gly Gly Leu Leu Leu	
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	gtacagagca aaacaacac aaaaaaacat aactatgtaa caaagagaat aactgctgct	940
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 Met Arg Ala Leu Pro Gly Leu Leu Glu Ala Arg Ala

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 20 Pro Ser Ser Ala Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro
 30 35 40
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 Pro Leu Arg Glu Glu Ile Met Ala Asn Asn Phe Ser Leu Glu Ser His
 45 50 55 60
 25 aac ata tca ctg act gaa cat tct agt atg cca gta gaa aaa aat atc 361
 Asn Ile Ser Leu Thr Glu His Ser Ser Met Pro Val Glu Lys Asn Ile
 65 70 75
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 Thr Leu Glu Arg Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr
 80 85 90
 30 tct ggg gat ttg aat gca gta aat gtg act tgg aaa aaa gat ggt gaa 457
 Ser Gly Asp Leu Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Glu
 95 100 105
 caa ett gag aat aat tat ett gtc agt gca aca gga agc acc ttg tat 505
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	Thr Gln Tyr Arg Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr			
	125	130	135	140
5	tct tgt ttc ttt cga gag gaa aag gaa caa agg gga aca ttt aat ttc			601
	Ser Cys Phe Phe Arg Glu Glu Lys Glu Gln Arg Gly Thr Phe Asn Phe			
	145	150	155	
	aaa gtc cct gaa ctt cat ggg aaa aac aag cca ttg atc tct tac gta			649
	Lys Val Pro Glu Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val			
10	160	165	170	
	ggg gat tct act gtc ttg aca tgt aaa tgt caa aat tgt ttt cct tta			697
	Gly Asp Ser Thr Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu			
	175	180	185	
	aat tgg acc tgg tac agt agt aat ggg agt gta aag gtt cct gtt ggt			745
15	Asn Trp Thr Trp Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly			
	190	195	200	
	gtt caa atg aat aaa tat gtg atc aat gga aca tat gct aac gaa aca			793
	Val Gln Met Asn Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr			
	205	210	215	220
20	aag ctg aag ata aca caa ctt ttg gag gaa gat ggg gaa tct tac tgg			841
	Lys Leu Lys Ile Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp			
	225	230	235	
	tgc cgt gca cta ttc caa tta ggc gag agt gaa gaa cac att gag ctt			889
	Cys Arg Ala Leu Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu			
25	240	245	250	
	gtg gtg ctg agc tat ttg gtg ccc ctc aaa cca ttt ctt gta ata gtg			937
	Val Val Leu Ser Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val			
	255	260	265	
	gct gag gtg att ctt tta gtg gcc acc att ctg ctt tgt gaa aag tac			985
30	Ala Glu Val Ile Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr			
	270	275	280	
	aca caa aag aaa aag aag cac tca gat gag ggg aaa gaa ttt gag cag			1033
	Thr Gln Lys Lys Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln			
	285	290	295	300
35	att gaa cag ctg aaa tca gat gat agc aat ggt ata gaa aat aat gtc			1081

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Ile Glu Gln Leu Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn Asn Val
 305 310 315
 ccc agg cat aga aaa aat gag tct ctg ggc cag tgaatacaaa acatca 1130
 Pro Arg His Arg Lys Asn Glu Ser Leu Gly Gln
 5 320 325
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 cataaaagca atgtaaatca gaataaatat gttagaccag aataaaatta attatattct 1370
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 Met Lys Phe Val Pro Cys Leu Leu Leu Val Thr Leu Ser Cys Leu
 30 1 5 10 15
 ggg act ttg ggt cag gcc ccg agg caa aag caa gga agc act ggg gag 154
 Gly Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Glu
 20 25 30
 gaa ttc cat ttc cag act gga ggg aga gat tcc tgc act atg cgt ccc 202
 35 Glu Phe His Phe Gln Thr Gly Gly Arg Asp Ser Cys Thr Met Arg Pro

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	agc agc ttg ggg caa ggt gct gga gaa gtc tgg ctt cgc gtc gac tgc	250		
	Ser Ser Leu Gly Gln Gly Ala Gly Glu Val Trp Leu Arg Val Asp Cys			
	50	55	60	
5	cgc aac aca gac cag acc tac tgg tgt gag tac agg ggg cag ccc agc	298		
	Arg Asn Thr Asp Gln Thr Tyr Trp Cys Glu Tyr Arg Gly Gln Pro Ser			
	65	70	75	
	atg tgc cag gct ttc gct gct gac ccc aaa tct tac tgg aat caa gcc	346		
	Met Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala			
10	80	85	90	95
	ctg cag gag ctg agg cgc ctt cac cat gcg tgc cag ggg gcc ccg gtg	394		
	Leu Gln Glu Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val			
	100	105	110	
	ctt agg cca tcc gtg tgc agg gag gct gga ccc cag gcc cat atg cag	442		
15	Leu Arg Pro Ser Val Cys Arg Glu Ala Gly Pro Gln Ala His Met Gln			
	115	120	125	
	cag gtg act tcc agc ctc aag ggc agc cca gag ccc aac cag cag cct	490		
	Gln Val Thr Ser Ser Leu Lys Gly Ser Pro Glu Pro Asn Gln Gln Pro			
	130	135	140	
20	gag gct ggg acg cca tct ctg agg ccc aag gcc aca gtg aaa ctc aca	538		
	Glu Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr			
	145	150	155	
	gaa gca aca cag ctg gga aag gac tcg atg gaa gag ctg gga aaa gcc	586		
	Glu Ala Thr Gln Leu Gly Lys Asp Ser Met Glu Glu Leu Gly Lys Ala			
25	160	165	170	175
	aaa ccc acc acc cga ccc aca gcc aaa cct acc cag cct gga ccc agg	634		
	Lys Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg			
	180	185	190	
	ccc gga ggg aat gag gaa gca aag aag gcc tgg gaa cat tgt tgg	682		
30	Pro Gly Gly Asn Glu Glu Ala Lys Lys Lys Ala Trp Glu His Cys Trp			
	195	200	205	
	aaa ccc ttc cag gcc ctg tgc gcc ttt ctc atc agc ttc ttc cga ggg	730		
	Lys Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly			
	210	215	220	
35	tgacagggtga aagaccoccta cagatctgac ctctcctga cagacaacca tctcttttta	790		

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	tattatgcgc ctttcaatcc aacgttctca cactggaaga agagagtttc taatcagatg	850
	caacggccca aattcttgat ctgcagcttc tctgaagttt ggaaaagaaa ccttcctttc	910
	tggagtttgc agagttcagc aatatgatag ggaacaggcg ctgatggggc caagagtgc	970
	aagcatacac aactacttat tatctgtaga agttttgctt tgttgatctg agccttctat	1030
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	Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Glu Ala Ser	
	5 10 15 20	
	gcc aat ctg gcc gcc gtg ccc agc aag aga tta aag atg cag tac gcc	150
	Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala	
25	25 30 35	
	acg ggg ccg ctg ctc aag ttc cag att tgt gtt tcc tgag	190
	Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser	
	40 45	
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30	gcattgaagg agagaattac ctccctcaac caatatatag acacatagca tctttcctgt	310
	cagtcttcaa actagtatta ataggcttaa taattgttgg caaggatcct tttgctttct	370
	ttggcatgca agctcctagc atctggcagt ggggcccaaga aaataaggtt tatgcatgta	430
	tgatggtttt cttcttgagc aacatgattg agaaccagtg tatgtcaaca ggtgcatttg	490
	agataaacttt aaatgatgta cctgtgtggt ctaagctgga atctgggtcac cttccatcca	550
35	tgcacaactt tgttcaaatt cttgacaatg aaatgaagct caatgtgcac atggattcaa	610

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	tcccacacca tgcgcatag caccacctat cagcactgaa aactcttttg cattaagggga	670
	tcattgcaag agcagcgtga ctgacattat gaaggcctgt actgaagaca gcaagctgtt	730
	agtacagacc agatgcttcc ttggcaggct cgttgctacat cttggaaaaac ctcaatgcaa	790
	gatagtgttt cagtgtgtgc atatttttga attctgcaca ttcatggagt gcaataatac	850
5	tgtatagctt tccccacctc ccacaaaatc acccagttaa tgtgtgtgtg tgtttttttt	910
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	attgagttac aatttgattt tttttccaaa gatgtctgtt aaatctgttg tgcttttata	1030
	tgaatatttg ttttttatag tttaaaattg atcctttggg aatccagttg aagttcccaa	1090
	atactttata agagtttata agacatctct aatttggcca tgcacagttt atacagttta	1150
10	caaaatatag cagatgcaag attatggggg aaatctata ttcagagtac tctataaatt	1210
	tttgtgtatg tgtgtatgtg cgtgtgatta ccagagaaact actaaaaaaa ccaactgctt	1270
	tttaaatcct attgtgtagt taaagtgtca tgccttgacc aatctaataga attgattaat	1330
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	tgg acc aag tac cag ctg ttc ctg gcc ggg ctc atg ctt gtt acc ggc	104
	Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val Thr Gly	
	5 10 15	
30	tcc atc aac acg ctc tcg gca aaa tgg gcg gac aat ttc atg gcc gag	152
	Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met Ala Glu	
	20 25 30	
	ggc tgt gga ggg agc aag gag cac agc ttc cag cat ccc ttc ctc cag	200
	Gly Cys Gly Gly Ser Lys Glu His Ser Phe Gln His Pro Phe Leu Gln	
35	35 40 45 50	

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	gca gtg ggc atg ttc ctg gga gaa ttc toc tgc ctg gct gcc ttc tac	248
	Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala Phe Tyr	
	55 60 65	
	ctc ctc cga tgc aga gct gca ggg caa tca gac toc agc gta gac ccc	296
5	Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Ser Val Asp Pro	
	70 75 80	
	cag cag ccc ttc aac cct ctt ctt ttc ctg ccc cca gcg ctc tgt gac	344
	Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Pro Ala Leu Cys Asp	
	85 90 95	
10	atg aca ggg acc agc ctc atg tat gtg gct ctg aac atg acc agt gcc	392
	Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr Ser Ala	
	100 105 110	
	ttc agc ttc cag atg ctg cgg ggt gca gtg atc ata ttc act gcc ctg	440
	Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Ile Phe Thr Gly Leu	
15	115 120 125 130	
	ttc tcg gtg gcc ttc ctg ggc cgg agg ctg gtg ctg agc cag tgg ctg	488
	Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln Trp Leu	
	135 140 145	
	ggc atc cta gcc acc atc gcg ggg ctg gtg gtc gtg ggc ctg gct gac	536
20	Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Val Gly Leu Ala Asp	
	150 155 160	
	ctc ctg agc aag cac gac agt cag cac aag ctc agc gaa gtg atc aca	584
	Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val Ile Thr	
	165 170 175	
25	ggg gac ctg ttg atc atc atg gcc cag atc atc gtt gcc atc cag atg	632
	Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile Gln Met	
	180 185 190	
	gtg cta gag gag aag ttc gtc tac aaa cac aat gtg cac cca ctg cgg	680
	Val Leu Glu Glu Lys Phe Val Tyr Lys His Asn Val His Pro Leu Arg	
30	195 200 205 210	
	gca gtt ggc act gag ggc ctc ttt ggc ttt gtg atc ctc tcc ctg ctg	728
	Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser Leu Leu	
	215 220 225	
	ctg gtg ccc atg tac tac atc ccc gcc ggc toc ttc agc gga aac cct	776
35	Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly Asn Pro	

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	230	235	240	
	cgt ggg aca ctg gag gat gca ttg gac gcc ttc tgc cag gtg ggc cag			824
	Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val Gly Gln			
	245	250	255	
5	cag cag ctc att gcc gtg gca ctg ctg ggc aac atc agc agc att gcc			872
	Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser Ile Ala			
	260	265	270	
	ttc ttc aac ttc gca ggc atc agc gtc acc aag gaa ctg agc gcc acc			920
	Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser Ala Thr			
10	275	280	285	290
	acc cgc atg gtg ttg gac agc ttg cgc acc gtt gtc atc tgg gca ctg			968
	Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp Ala Leu			
	295	300	305	
	agc ctg gca ctg ggc tgg gag gcc ttc cat gca ctg cag atc ctt ggc			1016
15	Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile Leu Gly			
	310	315	320	
	ttc ctc ata ctc ctt ata ggc act gcc ctc tac aat ggg cta cac cgt			1064
	Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu His Arg			
	325	330	335	
20	cag ctg ctg ggc cgc ctg tcc agg ggc cgg ccc ctg gca gag gag agc			1112
	Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu Glu Ser			
	340	345	350	
	gag cag gag aga ctg ctg ggt ggc acc cgc act ccc atc aat gat gcc			1160
	Glu Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn Asp Ala			
25	355	360	365	370
	agc tgagggtccc tggaggettc taactgcacc cgggtgctcc ttctccc			1210
	Ser			
	tgagactgag gccacacagg ctggtgggcc ccgaatgcc tatcccaag gcctcacct			1270
30	gtccctctcc tgcagaacct ccagggcagc tgcggccaca gaagataaca acaccaagt			1330
	cctctttttc tcaactaccac ctgcagggtg gtgttaccca gcccccacaa gcctgagtg			1390
	agtgcagac ctcagctctc tggaccctcc ctacagcact agagctaaat catgaagtg			1450
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<220>

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	1 5	
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	Trp Ala Ala Leu Leu Tyr Phe Tyr Gly Ile Ile Leu Asn Ser Ile Tyr	
	10 15 20	
15	cag tgc cct gag cac agt caa ctg aca act ctg ggc gtg gat ggg aag	150
	Gln Cys Pro Glu His Ser Gln Leu Thr Thr Leu Gly Val Asp Gly Lys	
	25 30 35	
	gag ttc cca gag gtc cac ttg ggc cag tgg tac ttt atc gca ggg gca	198
	Glu Phe Pro Glu Val His Leu Gly Gln Trp Tyr Phe Ile Ala Gly Ala	
20	40 45 50	
	gct ccc acc aag gag gag ttg gca act ttt gac cct gtg gac aac att	246
	Ala Pro Thr Lys Glu Glu Leu Ala Thr Phe Asp Pro Val Asp Asn Ile	
	55 60 65	
	gtc ttc aat atg gct gct ggc tct gcc ccg atg cag ctc cac ctt cgt	294
25	Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met Gln Leu His Leu Arg	
	70 75 80 85	
	gct acc atc cgc atg tgagtggaaa gatgggctct gtgtgcccg g	340
	Ala Thr Ile Arg Met	
	90	
30	aaatggatct accacctgac tgaagggagc acagatctca gaactgaagg ccgcectgac	400
	atgaagactg agctcttttc cagctcatgc ccagtggtgaa tcatgtgtgaa tgagacaggc	460
	cagggttacc agcgttttct cctctacaat cgtctaccac atctctccga aaagtgtgtg	520
	gaggaattca agtccctgac ttctgtgctg gactccaaag ccttcttatt gactcctagg	580
	aatcaagagg cctgtgagct gtccaataac tgacctgtaa ctctatctaa gtcccagat	640
35	qggtacaata qgaactgaat tatttgaagg aqaagctgga gacttccagc tccagctccc	700

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actcaagata ataaagataa tttttcaate ctc 733

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 tgggtgttcg ccaccccggg ccgcgtgagt ggggccccac gcagctcccc gcactcgtg 180
 15 ggccaacttg gccaaagcaac tctgtccggg gacgggtgct tgcggggggg gactaccggg 240
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 gcc atc ggg cgg cgg atc ttc gaa gtg ctg gag gag cca cac tgg aag 453
 Ala Ile Gly Ala Ala Ile Phe Glu Val Leu Glu Glu Pro His Trp Lys
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 25 gaq gcc aag aaa aac tac tac aca cag aag ctg cat ctg ctc aag gag 501
 Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Glu
 35 40 45
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 30 Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val
 50 55 60
 tct gat gct gca gga cag ggt gtg gcc atc aca ggg aac cag acc ttc 597
 Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe
 65 70 75 80
 35 aac aac tgg aac tgg ccc aat gca atg att ttt gca cgg acc gtc att 645

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	Thr Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg	
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	ctc ttc tgt gtt ttc tat ggt ctc ttc ggg gtg cgg ctc tgc ctg acg	741
	Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr	
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	tgg atc agt gcc ctg ggc aag ttc ttc ggg gga cgt gcc aag aga cta	789
10	Trp Ile Ser Ala Leu Gly Lys Phe Phe Gly Gly Arg Ala Lys Arg Leu	
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	ggg cag ttc ctt acc aag aga ggt gtg agt ctg cgg aag gcg cag atc	837
	Gly Gln Phe Leu Thr Lys Arg Gly Val Ser Leu Arg Lys Ala Gln Ile	
	145 150 155 160	
15	acg tgc aca gtc atc ttc atc gtg tgg ggc gtc cta gtc cac ctg gtg	885
	Thr Cys Thr Val Ile Phe Ile Val Trp Gly Val Leu Val His Leu Val	
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	atc cca ccc ttc gta ttc atg gtg act gag ggg tgg aac tac atc gag	933
	Ile Pro Pro Phe Val Phe Met Val Thr Glu Gly Trp Asn Tyr Ile Glu	
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	Gly Leu Tyr Tyr Ser Phe Ile Thr Ile Ser Thr Ile Gly Phe Gly Asp	
	195 200 205	
	ttt gtg gcc ggt gtg aac ccc agc gcc aac tac cac gcc ctg tac cgc	1029
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	210 215 220	
	tac ttc gtg gag ctc tgg atc tac ttg ggg ctg gcc tgg ctg tcc ctt	1077
	Tyr Phe Val Glu Leu Trp Ile Tyr Leu Gly Leu Ala Trp Leu Ser Leu	
	225 230 235 240	
30	ttt gtc aac tgg aag gtg agc atg ttt gtg gaa gtc cac aaa gcc att	1125
	Phe Val Asn Trp Lys Val Ser Met Phe Val Glu Val His Lys Ala Ile	
	245 250 255	
	aag aag cgg cgg cgg cga cgg aag gag tcc ttt gag agc tcc cca cac	1173
	Lys Lys Arg Arg Arg Arg Arg Lys Glu Ser Phe Glu Ser Ser Pro His	
35	260 265 270	

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	aac atc ttc agc ttt ctt tcc aag aag gaa gag acc tac aac gac etc	1269
5	Asn Ile Phe Ser Phe Leu Ser Lys Lys Glu Glu Thr Tyr Asn Asp Leu	
	290 295 300	
	atc aag cag atc ggg aag aag gcc atg aag aca agc ggg ggt ggg gag	1317
	Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu	
	305 310 315 320	
10	acg ggc cgg ggc cca ggg ctg ggg cct caa ggc ggt ggg etc cca gca	1365
	Thr Gly Pro Gly Pro Gly Leu Gly Pro Gln Gly Gly Gly Leu Pro Ala	
	325 330 335	
	ctg ccc cct tcc ctg gtg ccc ctg gta gtc tac tcc aag aac cgg gtg	1413
	Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val	
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	ccc acc ttg gaa gag gtg tca cag aca ctg agg agc aaa ggc cac gta	1461
	Pro Thr Leu Glu Glu Val Ser Gln Thr Leu Arg Ser Lys Gly His Val	
	355 360 365	
	tca agg tcc cca gat gag gag gct gtg gca cgg gcc cct gaa gac agc	1509
20	Ser Arg Ser Pro Asp Glu Glu Ala Val Ala Arg Ala Pro Glu Asp Ser	
	370 375 380	
	tcc cct gcc ccc gag gtg ttc atg aac cag ctg gac cgc atc agc gag	1557
	Ser Pro Ala Pro Glu Val Phe Met Asn Gln Leu Asp Arg Ile Ser Glu	
	385 390 395 400	
25	gaa tgc gag cca tgg gac gcc cag gac tac cac cca etc atc ttc cag	1605
	Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln	
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	gac gcc agc atc acc ttc gtg aac acg gag gct ggc etc tca gac gag	1653
	Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu	
30	420 425 430	
	gag acc tcc aag tcc tcg cta gag gac aac ttg gca ggg gag gag agc	1701
	Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Glu Ser	
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	ccc cag cag ggg gct gaa gcc aag gcg ccc ctg aac atg ggc gag ttc	1749
35	Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe	

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	ccc tcc tcc tcc gag tcc acc ttc acc agc act gag tct gag ctc tct			1797
	Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser			
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5	gtg cct tac gaa cag ctg atg aat gag tac aac aag gct aac agc ccc			1845
	Val Pro Tyr Glu Gln Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro			
		485	490	495
	aag ggc aca tgaggcaggg ccggtctcccc accccacett tgatgg			1890
	Lys Gly Thr			
10				
	cctcttcccc cctcacccta ggggtgtccc agatgaccgg gacgcctggc cctgtgtggg			1950
	ggggcagcct cggaactggg agtggggggc caggggcctt cctaaccctc catcatcccc			2010
	agctagatgt atgcccggga cagggcctct gttctccagc tgaaccatac cctggctgtg			2070
	ggggcatctg tctgagctt ggtgtgtgta tctacaatg caaagacatg ctggtgtggc			2130
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	ttggtggagt atcacacggt tctctgaggt cgggggcctc agctgtttaa gtttaaccgt			2250
	attaactgagc toggcatttg gagagggagc tctgaagtgt ctggggaggt accgctgtgc			2310
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20	gggagtgagg agatgagggc agggctctca acagtcctga ctcacagggc ctggaaacaa			2490
	gtcctatgtg ggcttggggc ctgggttctt catctcctt gttgtctac tcaggccacg			2550
	cccagagctg tgttccctgt ctcagggtcaa gcagtgccag acgcaaggct tctgtgtggc			2610
	ccccaaagtg taggagggag agtagcagag catgggttac tggaagccgg gactgtagg			2670
	gctgtgtggc agggagctgc aagagtgagg ctacgtctgt gctgtgtctg ccttaccctc			2730
25	tctgtcccg cggagaactg cacaccctgc ccgtggccc caggactgc actcccaatc			2790
	ctgtctctt ctcttccct gtgccctgaa caaggaccct actgcgccgc ttccctctcc			2850
	accagccccc ttgggccagg cagggtgagg ccaattgct cttggccac aaatgggtga			2910
	tggtcagata tgtgaatcaa gctcctttct ctacgtagt tttgatgtgc acgtgtgtgt			2970
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	ggcagaaact gctgtacta gatttctgtt gttctccatg atgttacc cttgggtgtgc			3150
	ccactgtgtc ctgaatgttt ttgttatatt ttgtttatt ttttaaaaca actgctgttt			3210
	ttatatacct ggaatctgtt gttggcttca gagccagtgg ttaaagagca ggggtcccaag			3270
	gattgggaga tctagtctct gccctcctgc cctgcaactc aattgggcct ttttcggtga			3330
35	cctcatccaa ggccatgatg tcaagggcc a tgtccccaag cagaggtgga gaaggggaca			3390

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ctgaggtgag caaaagcagg aaggggcac cactgcgggt gactggagge cgggcaggaa 3450
gcaagtcac agagccgctc agctccgttc actctctgcc ttctgcccca ctactgtggg 3510
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5 cctcgtatatt ttctgtgaaa tgttttaatg aaccatgttg ttgctggttg tcttgccatc 3690
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Asp Ser Lys Arg Gly Glu Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr
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cgg gag aag ctg aca ccc gag caa ctg cat tcc atg cgg cag gcg gag 149
25 Arg Glu Lys Leu Thr Pro Glu Gln Leu His Ser Met Arg Gln Ala Glu
                               30           35           40
ctt gcc cag tgg cag aag gtc cta cca cgg cgg cga acc cgg aac atc 197
Leu Ala Gln Trp Gln Lys Val Leu Pro Arg Arg Arg Thr Arg Asn Ile
                               45           50           55
gtg acc gcc cta gcc atc ggg gcc ctg gtg ttg gct att tat ggt tac 245
Val Thr Gly Leu Gly Ile Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr
                               60           65           70
acc ttc tac tgg att tcc cag gag cgt ttc cta gat gag cta gaa gac 293
Thr Phe Tyr Ser Ile Ser Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp
35 75           80           85           90

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	gag gcc aaa gct gcc cga gcc cga gct ctg gca agg gcg tca ggg tcc	341
	Glu Ala Lys Ala Ala Arg Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser	
	95 100 105	
	taatctgga tgggtattga tcatgtocaa cctgctggag ccccttcaca tgggtgatga	400
5	tgccccatga cctgtagaa attgaatcct gtcacaaca ttgttgacct tottactaac	460
	cttggaacct gattgagccc aagaaaccag gaacttacgc atttggccaa tgtcaaaaga	520
	acagaacctt gccactgca caettgctgt gtacaatgac tgagcccttt cttgtagttt	580
	gtttccttgt ttgagaggtg tgcctgcgac cgtggctttt cccaaagtgt ctgactttgt	640
	ggtttaccct cttcaccttc cagggacgca gttgttacga ggtagacgt ggcagctotg	700
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	gct tac aac aac ata acc ggc agg caa gat gaa act cat ttc aca gtt	161
	Ala Tyr Asn Asn Ile Thr Gly Arg Gln Asp Glu Thr His Phe Thr Val	
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	atc atc act tcc gta gga ctg gag aag ctt gca cag aaa gga aaa tca	209
30	Ile Ile Thr Ser Val Gly Leu Glu Lys Leu Ala Gln Lys Gly Lys Ser	
	25 30 35	
	ttg tca cct tta gca agt ata act gga ata tca cta ttt ttg att ata	257
	Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile Ser Leu Phe Leu Ile Ile	
	40 45 50	
35	tcc atg tgt ctt etc ttc cta tgg aaa aaa tat caa ccc tac aaa gtt	305

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Ser Met Cys Leu Leu Phe Leu Trp Lys Lys Tyr Gln Pro Tyr Lys Val
55 60 65 70
ata aaa cag aaa cta gaa ggc agg cca gaa aca gaa tac agg aaa gct 353
Ile Lys Gln Lys Leu Glu Gly Arg Pro Glu Thr Glu Tyr Arg Lys Ala
5 75 80 85
caa aca ttt tca ggc cat gaa gat gct ctg gat gac ttc gga ata tat 401
Gln Thr Phe Ser Gly His Glu Asp Ala Leu Asp Asp Phe Gly Ile Tyr
90 95 100
gaa ttt gtt gct ttt cca gat gtt tct ggt gtt tcc agg atc cca agc 449
10 Glu Phe Val Ala Phe Pro Asp Val Ser Gly Val Ser Arg Ile Pro Ser
105 110 115
agg tct gtt cca gcc tct gat tgt gta tcg ggg caa gat ttg cac agt 497
Arg Ser Val Pro Ala Ser Asp Cys Val Ser Gly Gln Asp Leu His Ser
120 125 130
15 aca gtg tat gaa gtt att cag cac atc cct gcc cag cag caa gac cat 545
Thr Val Tyr Glu Val Ile Gln His Ile Pro Ala Gln Gln Gln Asp His
135 140 145 150
cca gag tgaactttca tgggctaacc agtacattcg agtgaaattc tgaagaacc 600
Pro Glu
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atlttaagga aaaacagtgg aaaagtatat taatctggaa tcagtgaaga aaccaagacc 660
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gcaggttttt cagcatatac acaatgtctt gtgcaacaga aaaacatggt ggggaatat 780
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35 <212> PRT

WO 00/05367

PCT/JP99/03929

100/177

<213> Homo sapiens

<400> 91

Met Ala Pro Gln Asn Leu Ser Thr Phe Cys Leu Leu Leu Leu Tyr Leu
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 Ile Gly Ala Val Ile Ala Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val
 20 25 30
 Pro Arg Ser Ala Ser Ile Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu
 35 40 45
 Ala Leu Gln Leu His Pro Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln
 50 55 60
 Glu Lys Phe Gln Asp Leu Gly Ala Ala Tyr Glu Val Leu Ser Asp Ser
 65 70 75 80
 Glu Lys Arg Lys Gln Tyr Asp Thr Tyr Gly Glu Glu Gly Leu Lys Asp
 85 90 95
 Gly His Gln Ser Ser His Gly Asp Ile Phe Ser His Phe Phe Gly Asp
 100 105 110
 Phe Gly Phe Met Phe Gly Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile
 115 120 125
 Pro Arg Gly Ser Asp Ile Ile Val Asp Leu Glu Val Thr Leu Glu Glu
 130 135 140
 Val Tyr Ala Gly Asn Phe Val Glu Val Val Arg Asn Lys Pro Val Ala
 145 150 155 160
 Arg Gln Ala Pro Gly Lys Arg Lys Cys Asn Cys Arg Gln Glu Met Arg
 165 170 175
 Thr Thr Gln Leu Gly Pro Gly Arg Phe Gln Met Thr Gln Glu Val Val
 180 185 190
 Cys Asp Glu Cys Pro Asn Val Lys Leu Val Asn Glu Glu Thr Leu
 195 200 205
 Glu Val Glu Ile Glu Pro Gly Val Arg Asp Gly Met Glu Tyr Pro Phe
 210 215 220
 Ile Gly Glu Gly Glu Pro His Val Asp Gly Glu Pro Gly Asp Leu Arg
 225 230 235 240
 Phe Arg Ile Lys Val Val Lys His Pro Ile Phe Glu Arg Arg Gly Asp
 245 250 255

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Asp Leu Tyr Thr Asn Val Thr Ile Ser Leu Val Glu Ser Leu Val Gly
 260 265 270
 Phe Glu Met Asp Ile Thr His Leu Asp Gly His Lys Val His Ile Ser
 275 280 285
 5 Arg Asp Lys Ile Thr Arg Pro Gly Ala Lys Leu Trp Lys Lys Gly Gly
 290 295 300
 Gly Leu Pro Asn Phe Asp Asn Asn Asn Ile Lys Gly Ser Leu Ile Ile
 305 310 315 320
 Thr Phe Asp Val Asp Phe Pro Lys Glu Gln Leu Thr Glu Glu Ala Arg
 325 330 335
 10 Glu Gly Ile Lys Gln Leu Leu Lys Gln Gly Ser Val Gln Lys Val Tyr
 340 345 350
 Asn Gly Leu Gln Gly Tyr
 355
 15
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 <211> 226
 <212> PRT
 <213> Homo sapiens
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 <400> 92
 Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser Asn Ser Cys Cys
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 Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu Gly Val Trp Tyr
 20 25 30
 25 Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu Ser Ala Leu Ala
 35 40 45
 Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu Gly Gly Asp Phe
 50 55 60
 30 Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile Ala Ile Ser Leu
 65 70 75 80
 Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly Ala Tyr Lys Gln
 85 90 95
 Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln Ile Phe Asp Phe
 35 100 105 110

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Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile Tyr Pro Asn Ser
 115 120 125

Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe Pro Tyr Arg Asp
 130 135 140

5 Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu Ile Ile Leu Leu
 145 150 155 160

Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu Ile Ser Cys Val
 165 170 175

10 Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser Ser Asp Val Leu
 180 185 190

Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu Pro Pro Tyr Asp
 195 200 205

Asp Ala Thr Val Asn Gly Ala Ala Lys Glu Pro Pro Pro Tyr Val
 210 215 220

15 Ser Ala
 225

<210> 93
 <211> 195
 20 <212> PRT
 <213> Homo sapience

<400> 93

25 Met Arg Leu Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg
 1 5 10 15

Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys
 20 25 30

Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser
 35 40 45

30 Xaa Gly Tyr Arg Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln
 50 55 60

Arg Tyr Pro Asp Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro
 65 70 75 80

Ile Tyr Arg His Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu
 35 85 90 95

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Ile Gly Leu Ile Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met
 100 105 110

Gln Ala Pro Ser Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala
 115 120 125

5 Cys Met Met Val Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met
 130 135 140

Ser Thr Gly Ala Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser
 145 150 155 160

Lys Leu Glu Ser Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile
 10 165 170 175

Leu Asp Asn Glu Met Lys Leu Asn Val His Met Asp Ser Ile Pro His
 180 185 190

His Arg Ser
 195

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<210> 94
 <211> 339
 <212> PRT
 <213> Homo sapiens

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<400> 94

Met Asn Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu
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Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu
 25 20 25 30

Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu
 35 40 45

Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu
 50 55 60

30 Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser
 65 70 75 80

Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu
 85 90 95

Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu
 35 100 105 110

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Thr Asp Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu
 115 120 125
 Phe Gly Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg
 130 135 140
 5 Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu
 145 150 155 160
 Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His
 165 170 175
 Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu
 10 180 185 190
 Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His
 195 200 205
 Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr
 210 215 220
 15 Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn
 225 230 235 240
 Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn
 245 250 255
 Asn Gly Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu
 20 260 265 270
 Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu
 275 280 285
 Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp
 290 295 300
 25 Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe
 305 310 315 320
 Lys Ser Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr
 325 330 335
 Lys His Asp
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 <212> PRT
 <213> Homo sapience
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105/177

<400> 95

Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys
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Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro
 5 20 25 30

Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val
 35 40 45

Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser
 50 55 60

10 Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu
 65 70 75 80

Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe
 85 90 95

Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu
 15 100 105 110

Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala
 115 120 125

Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser
 130 135 140

20 Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu
 145 150 155 160

Ala Ala Val Ala Ala Leu Leu Leu Gly Val Val Ser Arg Glu Glu Val
 165 170 175

Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala
 25 180 185 190

Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile
 195 200 205

Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile
 210 215 220

30 Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val
 225 230 235 240

Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu
 245 250 255

Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala
 35 260 265 270

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Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro
 275 280 285
 Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser
 290 295 300
 5 Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro
 305 310 315 320
 Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg
 325 330 335
 10 Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu
 340 345 350
 Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser
 355 360 365
 Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Val Val Pro
 370 375 380
 15 Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser
 385 390 395 400
 Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu
 405 410 415
 20 Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu
 420 425 430
 Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu
 435 440 445
 Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe
 450 455 460
 25 Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Gly Ile Ser
 465 470 475 480
 Glu Leu Ala Ser Gly Pro Pro
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 35 <400> 96

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Met Arg Thr Leu Phe Asn Leu Leu Trp Leu Ala Leu Ala Cys Ser Pro
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 Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala Ala Ser Lys
 20 25 30
 5 Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp Lys Pro Val Gln Asp Arg
 35 40 45
 Gly Leu Val Val Thr Asp Leu Lys Ala Glu Ser Val Val Leu Glu His
 50 55 60
 Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp Arg His Phe Ala Gly Asp
 10 65 70 75 80
 Val Leu Gly Tyr Val Thr Pro Trp Asn Ser His Gly Tyr Asp Val Thr
 85 90 95
 Lys Val Phe Gly Ser Lys Phe Thr Gln Ile Ser Pro Val Trp Leu Gln
 100 105 110
 15 Leu Lys Arg Arg Gly Arg Glu Met Phe Glu Val Thr Gly Leu His Asp
 115 120 125
 Val Asp Gln Gly Trp Met Arg Ala Val Arg Lys His Ala Lys Gly Leu
 130 135 140
 His Ile Val Pro Arg Leu Leu Phe Glu Asp Trp Thr Tyr Asp Asp Phe
 20 145 150 155 160
 Arg Asn Val Leu Asp Ser Glu Asp Glu Ile Glu Glu Leu Ser Lys Thr
 165 170 175
 Val Val Gln Val Ala Lys Asn Gln His Phe Asp Gly Phe Val Val Glu
 180 185 190
 25 Val Trp Asn Gln Leu Leu Ser Gln Lys Arg Val Gly Leu Ile His Met
 195 200 205
 Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu Leu Ala Leu
 210 215 220
 Leu Val Ile Pro Pro Ala Ile Thr Pro Gly Thr Asp Gln Leu Gly Met
 30 225 230 235 240
 Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Val Leu Asp Gly Phe
 245 250 255
 Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ala His Gln Pro Gly Pro Asn
 260 265 270
 35 Ala Pro Leu Ser Trp Val Arg Ala Cys Val Gln Val Leu Asp Pro Lys

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275 280 285
 Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly Leu Asn Phe Tyr Gly Met
 290 295 300
 Asp Tyr Ala Thr Ser Lys Asp Ala Arg Glu Pro Val Val Gly Ala Arg
 5 305 310 315 320
 Tyr Ile Gln Thr Leu Lys Asp His Arg Pro Arg Met Val Trp Asp Ser
 325 330 335
 Gln Ala Ser Glu His Phe Phe Glu Tyr Lys Ser Arg Ser Gly Arg
 340 345 350
 10 His Val Val Phe Tyr Pro Thr Leu Lys Ser Leu Gln Val Arg Leu Glu
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 Leu Ala Arg Glu Leu Gly Val Gly Val Ser Ile Trp Glu Leu Gly Gln
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 Gly Leu Asp Tyr Phe Tyr Asp Leu Leu
 15 385 390

 <210> 97
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 20 <213> Homo sapience

 <400> 97
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 20 25 30
 Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro Gly Gly
 35 40 45
 Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile Thr Gly
 30 50 55 60
 Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln Val Lys
 65 70 75 80
 Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly Asn Thr
 85 90 95
 35 Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val Phe Val

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100 105 110
 Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser Lys Asp
 115 120 125
 Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser Ala Tyr
 5 130 135 140
 Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln Tyr Gln
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 Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro Leu Glu
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 Pro Val Gly Arg
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 35 40 45
 Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys Ser
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 Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val Ala
 30 65 70 75 80
 Ala Glu Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr Ser
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 Met Tyr Arg Glu Glu Phe Trp Ala Lys Pro Lys Pro
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<212> PRT

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<400> 99

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Arg Ser Ser Gly Gly Gly Gly Trp Ala Asp Pro Arg Thr Cys Leu Ser

35

40

45

Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala Trp Phe Val Phe Gln

50

55

60

15

Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln Tyr Gln Leu Leu Lys

65

70

75

80

Leu Glu Thr Asn Glu Phe Gln Gln Leu Gln Ser Lys Ile Ser Leu Ile

85

90

95

Ser Glu Lys Trp Gln Lys Ser Glu Ala Ile Met Glu Gln Leu Lys Ser

20

100

105

110

Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln Glu Glu Ile Asn Glu

115

120

125

Val Lys Thr Trp Ser Asn Arg Ile Thr Glu Lys Gln Asp Ile Leu Asn

130

135

140

25

Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr Lys Val Asp Gln Ser

145

150

155

160

Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys Ile Thr Ser Val Lys

165

170

175

Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr Asp Val Ile Ser Leu

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180

185

190

Thr Asp Ser Val Gln Glu Leu Glu Asn Lys Ile Glu Lys Val Glu Lys

195

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205

Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser Ser Ser Ile Asp Arg

210

215

220

35

Thr Ala Thr Leu Arg Lys Thr Ala Ser Glu Asn Ser Gln Arg Ile Asn

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 5 260 265 270
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 Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn Asp Leu Thr Leu Arg
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 10 Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg Glu Lys Glu Ile Ala
 305 310 315 320
 Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile Val Gln Ala Glu Ile
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 <211> 107
 <212> PRT
 20 <213> Homo sapience

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 35 40 45
 Ser Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val
 30 50 55 60
 Asn Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu
 65 70 75 80
 Leu Val Val Gly Gln Ala Pro Ala Trp Glu Gly Ser Leu Leu Arg Gly
 85 90 95
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100

105

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<211> 1074

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<212> DNA

<213> Homo Sapiens

<400> 101

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	gagaaacgga	aacagtacga	tacttatggt	gaagaaggat	taaaagatgg	tcatcagagc	300
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15	cctgtcagc	aagacagaaa	tattccaaga	ggaagtgata	ttattgtaga	tctagaagtc	420
	actttggaa	gagtatatgc	aggaaatttt	gtggaaagtg	ttagaacaaa	acctgtggca	480
	aggcagctc	ctggcaaacg	gaagtgcatt	tgtcggcaag	agatgcggac	caccagctg	540
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	aatgtgacaa	tctcattagt	tgagtcactg	gttgcttttg	agatggatat	tactcaactg	840
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	aagaaagggg	aggggctccc	caactttgac	aacaacaata	tcaagggttc	tttgataatc	960
25	acttttgatg	tgattttttc	aaaagaacag	ttaacagagg	aagcgagaga	aggtatcaaa	1020
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<211> 678

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<212> DNA

<213> Homo Sapiens

<400> 102

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<211> 585

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15 <213> Homo Sapience

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 25 aaccagtgta tgtcaacagg tgcatttgag ataactttaa atgatgtacc tgtgtggtct 480
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<210> 104

30 <211> 1017

<212> DNA

<213> Homo Sapience

<400> 104

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	ggaattggtg agggagctggc ttaccagttg tctaaactag gagtttctct tgtgtgctca	240
	gccagaagag tgcatagact ggaagggtg aaaagaagat gcctagagaa tggcaattta	300
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	gctaccaaag ctgtctctca ggagtttgtt agaatcgaca ttctgggtcaa caatggtgga	420
	atgtcccagc gttctctgtg catggatacc agcttggtatg tctacagaaa gctaatagag	480
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	aagcaaggaa agattgttac tgtgaatagc atcctgggta tcatatctgt acctctttcc	600
10	attggatact gtgctagcaa gcatgctctc cgggggtttt ttaatggcct tcgaacagaa	660
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	attgtggaga attccctagc tggagaagtc acaagacta taggcaataa tggagaccag	780
	tcaccaaga tgacaaccag tcgttgtgtg cggctgatgt taatcagcat ggccaatgat	840
	ttgaagaag tttgtagctc agaacaacct ttcttgttag taacatattt ttggcaatac	900
15	atgccaaacct gggcctggtg gataaccaac aagatgggga agaaaaggat tgagaacttt	960
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	accgcctggt ccataaggct tcaggtgacc gtgcccctca tgtttgcagg cctgggaactg	240
	tcctggggcc geatgcttct ggactatttc cagcactggc ctgtgtttgt ggaggtgaaa	300
	gaccttttga cattggtgcc gccctgggtg ggccctgaagg ggaacctgga gatgacactg	360
30	gcataccagc tctccacagc tgccaacact ggacaaattg atgaccccca ggagcagcac	420
	agagtcacga gcagcaacct ggcctcatc caggtgcagg ccaactgtctg ggggtcttg	480
	gctgctgtgg ctgcctgtct gttggggcgtg gtgtctctag aggaagtgga tgtcgcacag	540
	gtggagtgtc tgtgtgccag cagtgtctcc actgccttcc ttgcagcctt tgccctgggg	600
	gtgctgatgg tctgtatagt gattggtgct cgaaagctcg gggctcaacc agacaacatt	660
35	gccacgcccc tgcagccag cctggggagac ctcatcacac tgtccattct ggctttggtt	720

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	atcctgaagt ttggtggtt cccaatcacc ctggccatgg tcatcagcag ttctggagga	900
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	gtcataaaca gccagacott tgtggtgctc tacctgctgg caggcctgat ccaggtgaca	1260
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	tcagataagc cggtgcaaga cgggggtttg gtggtgacgg acctcaaage tgagagtgtg	180
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	ctctggccc tcttggtcat cccgcctgac atcaccctcg ggaaccagca gctgggcatg	720
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<211> 588

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25 <211> 321

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	Met Ala Pro Gln Asn Leu	
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	agc acc ttt tgc ctg ttg ctg cta tac ctc atc ggg gog gtg att gcc	223
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	Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val Pro Arg Ser Ala Ser Ile	
	25 30 35	
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	Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu Ala Leu Leu His Pro	
	40 45 50	
	gac cgg aac cct gat gat cca caa gcc cag gag aaa ttc cag gat ctg	367
	Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln Glu Lys Phe Gln Asp Leu	
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	Gly Ala Ala Tyr Glu Val Leu Ser Asp Ser Glu Lys Arg Lys Gln Tyr	
	75 80 85	
	gat act tat ggt gaa gaa tta aaa gat ggt cat cag agc tcc cat	463
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5	gga acc cct cgt cag caa gac aga aat att cca aga gga agt gat att			559
	Gly Thr Pro Arg Gln Gln Asp Arg Asn Ile Pro Arg Gly Ser Asp Ile			
	120	125	130	
	att gta gat cta gaa gtc act ttg gaa gaa gta tat gca gga aat ttt			607
	Ile Val Asp Leu Glu Val Thr Leu Glu Glu Val Tyr Ala Gly Asn Phe			
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	gtg gaa gta gtt aga aac aaa cct gtg gca agg cag gct cct ggc aaa			655
	Val Glu Val Val Arg Asn Lys Pro Val Ala Arg Gln Ala Pro Gly Lys			
	155	160	165	
	cgg aag tgc aat tgt cgg caa gag atg cgg acc acc cag ctg ggc cct			703
15	Arg Lys Cys Asn Cys Arg Gln Glu Met Arg Thr Thr Gln Leu Gly Pro			
	170	175	180	
	ggg cgc ttc caa atg acc cag gag gtg gtc tgc gac gaa tgc cct aat			751
	Gly Arg Phe Gln Met Thr Gln Glu Val Val Cys Asp Glu Cys Pro Asn			
	185	190	195	
20	gtc aaa cta gtg aat gaa gaa cga acg ctg gaa gta gaa ata gag cct			799
	Val Lys Leu Val Asn Glu Glu Arg Thr Leu Glu Val Glu Ile Glu Pro			
	200	205	210	
	ggg gtg aga gac ggc atg gag tac ccc ttt att gga gaa ggt gag cct			847
	Gly Val Arg Asp Gly Met Glu Tyr Pro Phe Ile Gly Glu Gly Glu Pro			
25	215	220	225	230
	cac gtg gat ggg gag cct gga gat tta cgg ttc cga atc aaa gtt gtc			895
	His Val Asp Gly Glu Pro Gly Asp Leu Arg Phe Arg Ile Lys Val Val			
	235	240	245	
	aag cac cca ata ttt gaa agg aga gga gat gat ttg tac aca aat gtg			943
30	Lys His Pro Ile Phe Glu Arg Arg Gly Asp Asp Leu Tyr Thr Asn Val			
	250	255	260	
	aca atc tca tta gtt gag tca ctg gtt ggc ttt gag atg gat att act			991
	Thr Ile Ser Leu Val Glu Ser Leu Val Gly Phe Glu Met Asp Ile Thr			
	265	270	275	
35	cac ttg gat ggt cac aag gta cat att tcc cgg gat aag atc acc agg			1039

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	His Leu Asp Gly His Lys Val His Ile Ser Arg Asp Lys Ile Thr Arg	
	280	285 290
	cca gga gcg aag cta tgg aag aaa ggg gaa ggg ctc ccc aac ttt gac	1087
	Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu Gly Leu Pro Asn Phe Asp	
5	295 300 305 310	
	aac aac aat atc aag ggc tct ttg ata atc act ttt gat gtg gat ttt	1135
	Asn Asn Asn Ile Lys Gly Ser Leu Ile Ile Thr Phe Asp Val Asp Phe	
	315 320 325	
	cca aaa gaa cag tta aca gag gaa gcg aga gaa ggt atc aaa cag cta	1183
10	Pro Lys Glu Gln Leu Thr Glu Glu Ala Arg Glu Gly Ile Lys Gln Leu	
	330 335 340	
	ctg aaa caa ggg tca gtg cag aag gta tac aat gga ctg caa gga tat	1231
	Leu Lys Gln Gly Ser Val Gln Lys Val Tyr Asn Gly Leu Gln Gly Tyr	
	345 350 355	
15	tgagagtga ataaaaattgg acttttgttta aaataagtga ataagcgata tttattatct	1290
	gcaaggtttt tttgtgtgtg tttttgtttt tatttttcaat atgcaagtta ggcttaattt	1350
	ttttatctaa tgatcatcat gaaatgaata agagggtcta agaatttgct catttgcaat	1410
	cggaagaaaa tgaccagcaa aaggtttact aatacctctc cctttgggga tttaatgtct	1470
	ggtgctgcgc cctgagtttc aagaattaaa gctgcaagag gactccagga gcaaaagaaa	1530
20	cacaatatag aggggttgag ttgttagcaa ttccattcaa aatgccaaact ggagaagtct	1590
	gtttttaaat acattttgtt gttattttt	1619
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	<211> 2054	
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	<213> Homo Sapience	
	<220>	
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	agcgaagggg accgaccggg cagaagctcg gagctctcgg ggtatcgagg aggcaggccc	120
	gcgggcgcac ggcgcagcgg gccgggagcc ggagcgccgg aggagccggc agcagcggcg	180
35	cggcgggctc caggcgaggc ggtcgacgct cctgaaaact tgcgcgcgcg ctgcggccac	240

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	tgcgcccgga gcg atg aag atg gtc gcg ccc tgg acg cgg ttc tac tcc	289
	Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser	
	1 5 10	
	aac agc tgc tgc ttg tgc tgc cat gtc cgc acc ggc acc atc ctg ctc	337
5	Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu	
	15 20 25	
	ggc gtc tgg tat ctg atc atc aat gct gtg gta ctg ttg att tta ttg	385
	Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val Leu Ile Leu Leu	
	30 35 40	
10	agt gcc ctg gct gat ccg gat cag tat aac ttt tca agt tct gaa ctg	433
	Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu	
	45 50 55 60	
	gga ggt gac ttt gag ttc atg gat gat gcc aac atg tgc att gcc att	481
	Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile	
15	65 70 75	
	gcg att tct ctt ctc atg atc ctg ata tgt gct atg gct act tac gga	529
	Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly	
	80 85 90	
	gcg tac aag caa cgc gca gcc tgg atc atc cca ttc ttc tgt tac cag	577
20	Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln	
	95 100 105	
	atc ttt gac ttt gcc ctg aac atg ttg gtt gca atc act gtg ctt att	625
	Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile	
	110 115 120	
25	tat cca aac tcc att cag gaa tac ata cgg caa ctg cct cct aat ttt	673
	Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe	
	125 130 135 140	
	ccc tac aga gat gat gtc atg tca gtg aat cct acc tgt ttg gtc ctt	721
	Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu	
30	145 150 155	
	att att ctt ctg ttt att agc att atc ttg act ttt aag ggt tac ttg	769
	Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu	
	160 165 170	
	att agc tgt gtt tgg aac tgc tac cga tac atc aat ggt agg aac tcc	817
35	Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser	

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	175	180	185	
	tct gat gtc ctg gtt tat gtt acc agc aat gac act acg gtg ctg cta			865
	Ser Asp Val Leu Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu			
	190	195	200	
5	ccc ccg tat gat gat gcc act gtg aat ggt gct gcc aag gag cca ccg			913
	Pro Pro Tyr Asp Asp Ala Thr Val Asn Gly Ala Ala Lys Glu Pro Pro			
	205	210	215	220
	cca cct tac gtg tct gcc taagccttca agtgggcgga gctgagggc			960
	Pro Pro Tyr Val Ser Ala			
10	225			
	agcagcttga ctttgagac atctgagcaa tagttctgtt atttcacttt tgccatgagc			1020
	ctctctgagc ttgtttgttg ctgaaatgct acttttttaa atttagatgt tagattgaaa			1080
	actgtagttt tcaacatatz ctttctgtga acactgtgat agattaactg tagaattctt			1140
	cctgtacgat tggggatata atgggcttca ctaacctccc ctaggcattg aaacttcccc			1200
15	caaatctgat ggacctagaa gtctgctttt gtacctgctg ggcgccaaag ttgggcattt			1260
	ttctctctgt tccctctctt ttgaaaatgt aaaaataaac caaaaataga caacttttcc			1320
	ttcagccatt ccagcataga gaacaaaacc ttatggaaac aggaatgtca attgtgtaat			1380
	cattgttcta attaggtaaa tagaagtccc tatgtatgtg ttacaagaat tccccccaca			1440
	acatccttta tgactgaagt tcaatgacag tttgtgtttg gtggtaaagg attttctcca			1500
20	tggcctgaat taagaccatt agaaagcacc aggcctgtgg agcagtgtacc atctgctgac			1560
	tgttcttctg gatcttctgt ccaggggacat ggggtgacat gccctgtatg tgttagaggg			1620
	tggaatggat gtgtttggcg ctgcatggga tctgtgtccc ctcttctccc ggattcacat			1680
	cccccccag ggcctcgctt tactaagtgt tctgcctag attggttcaa ggaggtcatc			1740
	caactgaatt tatecaaggg aattgggata tatttgatat actctgccc aacaacatgg			1800
25	aaaagggttt tcttttcccc gcaagctaca tctactgct ttgaactccc aagtatgtct			1860
	agtcaccttt taaaatgtaa acattttcag aaaaatgagg attgcttccc ttgtatgcgc			1920
	tttttacctt gactacctga attgcaaggg atttttatat attcatatg tacaaagtca			1980
	gcaactctcc tgttggtcca ttattgaatg tctgtgtaaa taagtgtgtt gcaattaaaa			2040
	caaggtttgc ccac			2054
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	<211> 1380			
	<212> DNA			
	<213> Homo Sapiens			
35	<220>			

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<221> CDS

<222> (43)...(630)

<400> 113

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	Met Arg Leu Leu	
	1	
	ctg ctt ctc cta gtg gcg gcg tct gcg atg gtc cgg agc gag gcc tgc	102
	Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Glu Ala Ser	
10	5 10 15 20	
	gcc aat ctg ggc ggc gtg ccc agc aag aga tta aag atg cag tac gcc	150
	Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala	
	25 30 35	
	acg ggg cgg ctg ctc aag ttc cag att tgt gtt tcc tga ggt tat agg	198
15	Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser Xaa Gly Tyr Arg	
	40 45 50	
	cgg gtg ttt gag gag tac atg cgg gtt att agc cag cgg tac cca gac	246
	Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln Arg Tyr Pro Asp	
	55 60 65	
20	atc cgc att gaa gga gag aat tac ctc cct caa cca ata tat aga cac	294
	Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro Ile Tyr Arg His	
	70 75 80	
	ata gca tct ttc ctg tca gtc ttc aaa cta gta tta ata ggc tta ata	342
	Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu Ile Gly Leu Ile	
25	85 90 95 100	
	att gtt ggc aag gat cct ttt gct ttc ttt ggc atg caa gct cct agc	390
	Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met Gln Ala Pro Ser	
	105 110 115	
	atc tgg cag tgg ggc caa gaa aat aag gtt tat gca tgt atg atg gtt	438
30	Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala Cys Met Met Val	
	120 125 130	
	ttc ttc ttg agc aac atg att gag aac cag tgt atg tca aca ggt gca	486
	Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met Ser Thr Gly Ala	
	135 140 145	
35	ttt gag ata act tta aat gat gta cct gtg tgg tct aag ctg gaa tct	534

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Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser Lys Leu Glu Ser
 150 155 160
 ggt cac ctt cca toc atg caa caa ctt gtt caa att ctt gac aat gaa 582
 Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile Leu Asp Asn Glu
 5 165 170 175 180
 atg aag ctc aat gtg cat atg gat tca atc cca cac cat cga tca 627
 Met Lys Leu Asn Val His Met Asp Ser Ile Pro His His Arg Ser
 185 190 195
 tag caccacctat cagcaactgaa aactottttg cattaaggga tcattgcaag 680
 10 agcagcgtga ctgacattat gaaggcctgt actgaagaca gcaagctgtt agtacagacc 740
 agatgctttc ttggcaggct cgttgtacct cttggaanaac ctcaatgcaa gatagtgtt 800
 cagtgtgtgc atatttttga attctgcaca ttcattgagt gcaataatac tgtatagctt 860
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 15 aatttgattt tttttccaaa gatgtctgtt aaatctgttg tgcttttata tgaatatttg 1040
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 agagtttatc agacatctct aatttggcca tgtccagttt atacagttta caaaatatag 1160
 cagatgcaag attatggggg aaatctata ttcagagtac tctataaatt tttgtgtatg 1220
 tgtgtatgtg cgtgtgatta ccagagaact actaaaaaaa ccaactgctt tttaaactct 1280
 20 attgtgtagt taaagtgtca tgccttgacc aatctaatag attgattaat taactgggac 1340
 tttatactta actaaataaa aaactaagca gatattgagtt 1380

<210> 114

<211> 1292

25 <212> DNA

<213> Homo Sapiens

<220>

<221> CDS

<222> (113)...(1132)

30

<400> 114

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 gactctggtg cgggcgctct tcttcccccc gagctggggc tgcgcggcgc ca atg aac 118

Met Asn

35

1

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	tgg gag ctg ctg ctg tgg ctg ctg gtg ctg tgc gcg ctg ctc ctg ctc	166
	Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu Leu	
	5 10 15	
	tgt gtg cag ctg ctg cgc ttc ctg agg gct gac ggc gac ctg acg cta	214
5	Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu Thr Leu	
	20 25 30	
	cta tgg gcc gag tgg cag gga cga cgc cca gaa tgg gag ctg act gat	262
	Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu Thr Asp	
	35 40 45 50	
10	atg gtg gtg tgg gtg act gga gcc tcg agt gga att ggt gag gag ctg	310
	Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu	
	55 60 65	
	gct tac cag ttg tct aaa cta gga gtt tct ctt gtg ctg tca gcc aga	358
	Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser Ala Arg	
15	70 75 80	
	aga gtg cat gag ctg gaa agg gtg aaa aga aga tgc cta gag aat ggc	406
	Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu Asn Gly	
	85 90 95	
	aat tta aaa gaa aaa gat ata ctt gtt ttg ccc ctt gac ctg acc gac	454
20	Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu Thr Asp	
	100 105 110	
	act ggt tcc cat gaa gcg gct acc aaa gct gtt ctc cag gag ttt ggt	502
	Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu Phe Gly	
	115 120 125 130	
25	aga atc gac att ctg gtc aac aat ggt gga atg tcc cag cgt tct ctg	550
	Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg Ser Leu	
	135 140 145	
	tgc atg gat acc agc ttg gat gtc tac aga aag cta ata gag ctt aac	598
	Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu Leu Asn	
30	150 155 160	
	tac tta ggg acg gtg tcc ttg aca aaa tgt gtt ctg cct cac atg atc	646
	Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His Met Ile	
	165 170 175	
	gag agg aag caa gga aag att gtt act gtg aat agc atc ctg ggt atc	694
35	Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu Gly Ile	

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	180	185	190	
	ata tct gta cct ctt tcc att gga tac tgt gct agc aag cat gct ctc			742
	Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His Ala Leu			
	195	200	205	210
5	cgg ggt ttt ttt aat ggc ctt cga aca gaa ctt gcc aca tac cca ggt			790
	Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr Pro Gly			
	215	220	225	
	ata ata gtt tct aac att tgc cca gga cct gtg caa tca aat att gtg			838
	Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn Ile Val			
10	230	235	240	
	gag aat tcc cta gct gga gaa gtc aca aag act ata ggc aat aat gga			886
	Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn Asn Gly			
	245	250	255	
	gac cag tcc cac aag atg aca acc agt cgt tgt gtg cgg ctg atg tta			934
15	Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu Met Leu			
	260	265	270	
	atc agc atg gcc aat gat ttg aaa gaa gtt tgg atc tca gaa caa cct			982
	Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu Gln Pro			
	275	280	285	290
20	ttc ttg tta gta aca tat ttg tgg caa tac atg cca acc tgg gcc tgg			1030
	Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp Ala Trp			
	295	300	305	
	tgg ata acc aac aag atg ggg aag aaa agg att gag aac ttt aag agt			1078
	Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe Lys Ser			
25	310	315	320	
	ggt gtg gat gca gac tct tct tat ttt aaa atc ttt aag aca aaa cat			1126
	Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr Lys His			
	325	330	335	
	gac tgaaaagagc atctgtactt ttcaagccac tggagggaaa aatggaaaac a			1180
30	Asp			
	tgaaaacagc aatettotta tgctttctgaa taatcaaaga ctaatttgtg gttttacttt			1240
	ttaatagata tgactttgtt tccaacatgg aatgaaataa aaaataagta at			1292
35	<210> 115			

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127/177

<211> 2168

<212> DNA

<213> Homo Sapience

<220>

5 <221> CDS

<222> (56)...(1519)

<400> 115

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	Met Asp Gly Thr Glu Thr Arg Gln Arg Arg Leu Asp Ser Cys Gly Lys	
	1 5 10 15	
	cca ggg gag ctg ggg ctt cct cac ccc ctc agc aca gga gga ctc cct	151
	Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro	
15	20 25 30	
	gta gcc tca gaa gat gga gct ctc agg gcc cct gag agc caa agc gtg	199
	Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val	
	35 40 45	
	acc ccc aag cca ctg gag act gag cct agc agg gag acc gcc tgg tcc	247
20	Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser	
	50 55 60	
	ata ggc ctt cag gtg acc gtg ccc ttc atg ttt gca ggc ctg gga ctg	295
	Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu	
	65 70 75 80	
25	tcc tgg gcc ggc atg ctt ctg gac tat ttc cag cac tgg cct gtg ttt	343
	Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe	
	85 90 95	
	gtg gag gtg aaa gac ctt ttg aca ttg gtg ccg ccc ctg gtg ggc ctg	391
	Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu	
30	100 105 110	
	aag ggg aac ctg gag atg aca ctg gca tcc aga ctc tcc aca gct gcc	439
	Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala	
	115 120 125	
	aac act gga caa att gat gac ccc cag gag cag cac aga gtc atc agc	487
35	Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser	

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	130	135	140	
	agc aac ctg gcc ctc atc cag gtg cag gcc act gtc gtg ggg ctc ttg			535
	Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu			
	145	150	155	160
5	gct gct gtg gct gcg ctg ctg ttg gcc gtg gtg tct cga gag gaa gtg			583
	Ala Ala Val Ala Ala Leu Leu Leu Gly Val Val Ser Arg Glu Glu Val			
	165	170	175	
	gat gtc gcc aag gtg gag ttg ctg tgt gcc agc agt gtc ctc act gcc			631
	Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala			
10	180	185	190	
	ttc ctt gca gcc ttt gcc ctg ggg gtg ctg atg gtc tgt ata gtg att			679
	Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile			
	195	200	205	
	ggg gct cga aag ctc ggg gtc aac cca gac aac att gcc acg ccc att			727
15	Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile			
	210	215	220	
	gca gcc agc ctg gga gac ctc atc aca ctg tcc att ctg gct ttg gtt			775
	Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val			
	225	230	235	240
20	agc agc ttc ttc tac aga cac aaa gat agt cgg tat ctg acg ccg ctg			823
	Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu			
	245	250	255	
	gtc tgc ctc agc ttt gcg gct ctg acc cca gtg tgg gtc ctc att gcc			871
	Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala			
25	260	265	270	
	aag cag agc cca ccc atc gtg aag atc ctg aag ttt gcc tgg ttc cca			919
	Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro			
	275	280	285	
	atc atc ctg gcc atg gtc atc agc agt ttc gga gga ctc atc ttg agc			967
30	Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser			
	290	295	300	
	aaa acc gtt tct aaa cag cag tac aaa gcc atg gcg ata ttt acc ccc			1015
	Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro			
	305	310	315	320
35	gtc ata tgt ggt gtt ggt gcc aat ctg gtg gcc att cag acc agc cga			1063

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	Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg	
	325 330 335	
	atc tca acc tac ctg cac atg tgg agt gca cct ggc gtc ctg ccc ctc	1111
	Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu	
5	340 345 350	
	cag atg aag aaa ttc tgg ccc aac ccg tgt tct act ttc tgc acg tca	1159
	Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser	
	355 360 365	
	gaa atc aat tcc atg tca gct cga gtc ctg ctc ttg ctg gtg gtc cca	1207
10	Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Leu Val Val Pro	
	370 375 380	
	ggc cat ctg att ttc ttc tac atc atc tac ctg gtg gag ggt cag tca	1255
	Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser	
	385 390 395 400	
15	gtc ata aac agc cag acc ttt gtg gtg ctc tac ctg ctg gca ggc ctg	1303
	Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu	
	405 410 415	
	atc cag gtg aca atc ctg ctg tac ctg gca gaa gtg atg gtt cgg ctg	1351
	Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu	
20	420 425 430	
	act tgg cac cag gcc ctg gat cct gac aac cac tgc atc ccc tac ctt	1399
	Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu	
	435 440 445	
	aca ggg ctg ggg gac ctg ctc ggt act ggc ctc ctg gca ctc tgc ttt	1447
25	Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe	
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	ttc act gac tgg cta ctg aag agc aag gca gag ctg ggt ggc atc tca	1495
	Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Gly Ile Ser	
	465 470 475 480	
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	Glu Leu Ala Ser Gly Pro Pro	
	485	
	aatttccctct cacatcagtg ggatacagaa ttcagtttct cccctggccag gtccttggga	1610
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35	ctcggtctctg ggggtgatac ctgagcctgc aatagagccc tgaatcaag agcattggctt	1730

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	Met Arg Thr Leu Phe Asn Leu Leu Trp Leu	
	1 5 10	
	gcc ctg gcc tgc agc cct gtt cac act acc ctg tca aag tca gat gcc	158
	Ala Leu Ala Cys Ser Pro Val His Thr Thr Leu Ser Lys Ser Asp Ala	
25	15 20 25	
	aaa aaa gcc gcc tca aag acg ctg ctg gag aag agt cag ttt tca gat	203
	Lys Lys Ala Ala Ser Lys Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp	
	30 35 40	
	aag ccg gtg caa gac cgg ggt ttg gtg gtg acg gac ctc aaa gct gag	254
30	Lys Pro Val Gln Asp Arg Gly Leu Val Val Thr Asp Leu Lys Ala Glu	
	45 50 55	
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	Ser Val Val Leu Glu His Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp	
	60 65 70	
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5	His	Gly	Tyr	Asp	Val	Thr	Lys	Val	Phe	Gly	Ser	Lys	Phe	Thr	Gln	Ile	
					95					100					105		
	tca	ccc	gtc	tgg	ctg	cag	ctg	aag	aga	cgt	ggc	cgt	gag	atg	ttt	gag	446
	Ser	Pro	Val	Trp	Leu	Gln	Leu	Lys	Arg	Arg	Gly	Arg	Glu	Met	Phe	Glu	
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10	gtc	acg	ggc	ctc	cac	gac	gtg	gac	caa	ggg	tgg	atg	cga	gct	gtc	agg	494
	Val	Thr	Gly	Leu	His	Asp	Val	Asp	Gln	Gly	Trp	Met	Arg	Ala	Val	Arg	
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	aag	cat	gcc	aag	ggc	ctg	cac	ata	gtg	cct	cgg	ctc	ctg	ttt	gag	gac	542
	Lys	His	Ala	Lys	Gly	Leu	His	Ile	Val	Pro	Arg	Leu	Leu	Phe	Glu	Asp	
					140					145					150		
15	tgg	act	tac	gat	gat	ttc	cgg	aac	gtc	tta	gac	agt	gag	gat	gag	ata	590
	Trp	Thr	Tyr	Asp	Asp	Phe	Arg	Asn	Val	Leu	Asp	Ser	Glu	Asp	Glu	Ile	
						155					160				165		
	gag	gag	ctg	agc	aag	acc	gtg	gtc	cag	gtg	gca	aag	aac	cag	cat	ttc	638
	Glu	Glu	Leu	Ser	Lys	Thr	Val	Val	Gln	Val	Ala	Lys	Asn	Gln	His	Phe	
20						175					180				185		
	gat	ggc	ttc	gtg	gtg	gag	gtc	tgg	aac	cag	ctg	cta	agc	cag	aag	cgc	686
	Asp	Gly	Phe	Val	Val	Glu	Val	Trp	Asn	Gln	Leu	Leu	Ser	Gln	Lys	Arg	
						190					195				200		
25	gtg	ggc	ctc	atc	cac	atg	ctc	acc	cac	ttg	gcc	gag	gct	ctg	cac	cag	734
	Val	Gly	Leu	Ile	His	Met	Leu	Thr	His	Leu	Ala	Glu	Ala	Leu	His	Gln	
						205					210				215		
	gcc	cgg	ctg	ctg	gcc	ctc	ctg	gtc	atc	ccg	cct	gcc	atc	acc	ccc	ggg	782
	Ala	Arg	Leu	Leu	Ala	Leu	Leu	Val	Ile	Pro	Pro	Ala	Ile	Thr	Pro	Gly	
						220					225				230		
30	acc	gac	cag	ctg	ggc	atg	ttc	acg	cac	aag	gag	ttt	gag	cag	ctg	gcc	830
	Thr	Asp	Gln	Leu	Gly	Met	Phe	Thr	His	Lys	Glu	Phe	Glu	Gln	Leu	Ala	
						235					240				245		
	ccc	gtg	ctg	gat	ggt	ttc	agc	ctc	atg	acc	tac	gac	tac	tct	aca	gcg	878
	Pro	Val	Leu	Asp	Gly	Phe	Ser	Leu	Met	Thr	Tyr	Asp	Tyr	Ser	Thr	Ala	
35						255					260				265		

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cat cag cct ggc cct aat gca ccc ctg tcc tgg gtt cga gcc tgc gtc 926
 His Gln Pro Gly Pro Asn Ala Pro Leu Ser Trp Val Arg Ala Cys Val
 270 275 280

cag gtc ctg gac cag aag tcc aag tgg cga agc aaa atc ctc ctg ggg 974
 5 Gln Val Leu Asp Pro Lys Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly
 285 290 295

ctc aac ttc tat ggt atg gac tac gcg acc tcc aag gat gcc cgt gag 1022
 Leu Asn Phe Tyr Gly Met Asp Tyr Ala Thr Ser Lys Asp Ala Arg Glu
 300 305 310

cct gtt gtc ggg gcc agg tac atc cag aca ctg aag gac cac agg ccc 1070
 10 Pro Val Val Gly Ala Arg Tyr Ile Gln Thr Leu Lys Asp His Arg Pro
 315 320 325 330

cgg atg gtg tgg gac agc cag gcc tca gag cac ttc ttc gag tac aag 1118
 Arg Met Val Trp Asp Ser Gln Ala Ser Glu His Phe Phe Glu Tyr Lys
 15 335 340 345

aag agc cgc agt ggg agg cac gtc gtc ttc tac cca acc ctg aag tcc 1166
 Lys Ser Arg Ser Gly Arg His Val Val Phe Tyr Pro Thr Leu Lys Ser
 350 355 360

ctg cag gtg cgg ctg gag ctg gcc cgg gag ctg ggc gtt ggg gtc tot 1214
 20 Leu Gln Val Arg Leu Glu Leu Ala Arg Glu Leu Gly Val Gly Val Ser
 365 370 375

atc tgg gag ctg ggc cag gcc ctg gac tac ttc tac gac ctg ctc t 1260
 Ile Trp Glu Leu Gly Gln Gly Leu Asp Tyr Phe Tyr Asp Leu Leu
 380 385 390

agggtggcgaat tgcggcctcc gcggtggagcgt tgtttttttc taagccatgg agtgagtgag 1320
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Glu Ser Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Leu Thr
15 20 25 30
ctt gcc ctc ctg ggg ggc ccc acc tgg gca ggg aag atg tat ggc cct 145
Leu Ala Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro
10 35 40 45
gga gga ggc aag tat, ttc agc acc act gaa gac tac gac cat gaa atc 193
Gly Gly Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile
50 55 60
aca ggg ctg cgg gtg tct gta ggt ctt ctc ctg gtg aaa agt gtc cag 241
15 Thr Gly Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln
65 70 75
gtg aaa ctt gga gac tcc tgg gac gtg aaa ctg gga gcc tta ggt ggg 289
Val Lys Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly
80 85 90
20 aat acc cag gaa gtc acc ctg cag cca ggc gaa tac atc aca aaa gtc 337
Asn Thr Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val
95 100 105 110
ttt gtc gcc ttc caa gct ttc ctc cgg ggt atg gtc atg tac acc agc 385
Phe Val Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser
25 115 120 125
aag gac cgc tat ttc tat ttt ggg aag ctt gat ggc cag atc tcc tct 433
Lys Asp Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser
130 135 140
gcc tac ccc agc caa gag ggg cag gtg ctg gtg ggc atc tat ggc cag 481
30 Ala Tyr Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln
145 150 155
tat caa ctc ctt ggc atc aag agc att ggc ttt gaa tgg aat tat cca 529
Tyr Gln Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro
160 165 170
35 cta gag gag ccg acc act gag cca cca gtt aat ctc aca tac tca gca 577

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Leu Glu Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala
 175 180 185 190
 aac tca ccc gtg ggt cgc taggggtggg tatggggcca tccgagctga ggcca 630
 Asn Ser Pro Val Gly Arg
 5 195
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 gaggagtgg gagccgagc ctagggtcct tcgggtgagg ggagacggag ccagcgagga 240
 g atg gag cag aag ctt gtg gag gag att ctt caa gca atc act atg 286
 Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met
 1 5 10 15
 25 tca aca gac aca ggt gtt tcc ctt cct tca tat gag gaa gat cag gga 334
 Ser Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly
 20 25 30
 tca aaa ctc att cga aaa gct aaa gag gca cca ttc gta ccc gtt gga 382
 Ser Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly
 30 35 40 45
 ata gcg ggt ttt gca gca att gtt gca tat gga tta tat aaa ctg aag 430
 Ile Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys
 50 55 60
 agc agg gga aat act aaa atg tcc att cat ctg atc cac atg cgt gtg 478
 35 Ser Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val

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	65	70	75	
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	Ala Ala Gln Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr			
	80	85	90	95
5	tcc atg tat cgg gaa ttc tgg gca aaa cct aag cct tagaagaa			570
	Ser Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro			
	100	105		
	gagatgetgt cttggtcttg ttggaggagc ttgctttagt tagatgtctt attattaaag			630
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	Met Ser Glu Val Lys Ser Arg Lys Lys Ser Gly			
	1	5	10	
	ccc aag gga gcc cct gct gcg gag ccc ggg aag cgg agc gag ggc ggg			158
25	Pro Lys Gly Ala Pro Ala Ala Glu Pro Gly Lys Arg Ser Glu Gly Gly			
	15	20	25	
	aag acc ccc gtg gcc cgg agc agc gga ggc ggg ggc tgg gca gac ccc			206
	Lys Thr Pro Val Ala Arg Ser Ser Gly Gly Gly Trp Ala Asp Pro			
	30	35	40	
30	cga acg tgc ctg agc ctg ctg tgc ctg ggg acg tgc ctg ggc ctg gcc			254
	Arg Thr Cys Leu Ser Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala			
	45	50	55	
	tgg ttt gta ttt cag cag tca gaa aaa ttt gca aag gtg gaa aac caa			302
	Trp Phe Val Phe Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln			
35	60	65	70	75

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	tac cag tta ctg aaa cta gaa acc aat gaa ttc caa caa ctt caa agt	350
	Tyr Gln Leu Leu Lys Leu Glu Thr Asn Glu Phe Gln Gln Leu Gln Ser	
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	aaa atc agt tta att tca gaa aag tgg cag aaa tct gaa gct atc atg	398
5	Lys Ile Ser Leu Ile Ser Glu Lys Trp Gln Lys Ser Glu Ala Ile Met	
	95 100 105	
	gaa caa ttg aag tct ttt caa ata att gct cat cta aag cgt cta cag	446
	Glu Gln Leu Lys Ser Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln	
	110 115 120	
10	gaa gaa att aat gag gta aaa act tgg tcc aat agg ata act gaa aaa	494
	Glu Glu Ile Asn Glu Val Lys Thr Trp Ser Asn Arg Ile Thr Glu Lys	
	125 130 135	
	cag gat ata ctg aac aac agt ctg acg acg ctt tct caa gac att aca	542
	Gln Asp Ile Leu Asn Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr	
15	140 145 150 155	
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	att aca agt gta aaa aca gat ata cga cgg att tca ggt tta gta act	638
20	Ile Thr Ser Val Lys Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr	
	175 180 185	
	gat gta ata tca ttg aca gat tct gtg caa gaa cta gaa aat aaa ata	686
	Asp Val Ile Ser Leu Thr Asp Ser Val Gln Glu Leu Glu Asn Lys Ile	
	190 195 200	
25	gag aaa gta gaa aaa aat aca gta aaa aat ata ggt gat ctt ctt tca	734
	Glu Lys Val Glu Lys Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser	
	205 210 215	
	agc agt att gat cga aca gca acg ctc cga aag aca gca tct gaa aat	782
	Ser Ser Ile Asp Arg Thr Ala Thr Leu Arg Lys Thr Ala Ser Glu Asn	
30	220 225 230 235	
	tca caa aga att aac tct gtt aag aag acg cta acc gaa cta aag agt	830
	Ser Gln Arg Ile Asn Ser Val Lys Lys Thr Leu Thr Glu Leu Lys Ser	
	240 245 250	
	gac ttc gac aaa cat aca gat aga ttt cta agc tta gaa ggt gac aga	878
35	Asp Phe Asp Lys His Thr Asp Arg Phe Leu Ser Leu Glu Gly Asp Arg	

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	255	260	265	
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	270	275	280	
5	gtg tat aat cta aag aag gac ttt tcc cgt tta gaa cca tta gta aat	974		
	Val Tyr Asn Leu Lys Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn			
	285	290	295	
	gat tta aca cta cgc att ggg aga ttg gtt acc gac tta cta caa aga	1022		
	Asp Leu Thr Leu Arg Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg			
10	300	305	310	315
	gag aaa gaa att gct ttc tta agt gaa aaa ata tct aat tta aca ata	1070		
	Glu Lys Glu Ile Ala Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile			
	320	325	330	
	gtc caa gct gag att aag gat att aaa gat gaa ata gca cac att tca	1118		
15	Val Gln Ala Glu Ile Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser			
	335	340	345	
	gat atg aat tagtttgaca ttattgagat tagactaagg taattttttt aat	1170		
	Asp Met Asn			
	350			
20	gggacctctc atgagaagac tggtaaatca aaaataatga tattttggag caaaagtcac	1230		
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35	aacacagctg gtatttcaag tctcctggga cctcactcag gaatgatacc cctcagtag	180		

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	aagcagcagg tgatcttaac tcctttcaaa gagcaggcct gtctgggaag cc atg	235
	Met	
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5	Ser Ser Ala Gly Thr Ala Thr Pro Leu Glu Met Asp His Lys Leu Thr	
	5 10 15	
	tct cag cca ggc agg cca agc ttc tat tgt aac agt agg cac agt ata	331
	Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser Ile	
	20 25 30	
10	gtc gga tca tca cat cag ctg ggt ttt tgg ttt agt cat cta gag tgc	379
	Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Glu Ser	
	35 40 45	
	tct gga cta aag gtc ttt cag gtc tcc ttg ccc tgt gag tgc gtg aac	427
	Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val Asn	
15	50 55 60 65	
	ctc ccc acc cga att gcc tca gtt gtc ctg agc ctc atg tet ctc ctg	475
	Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu Leu	
	70 75 80	
	gtg gtg ggc cag gcc cct gca tgg gaa ggg agc ctg ctg cgg ggc agg	523
20	Val Val Gly Gln Ala Pro Ala Trp Glu Gly Ser Leu Leu Arg Gly Arg	
	85 90 95	
	cca gct ggg ggt gct cac cta tgc gca gca tgaagttatt gaaggac	570
	Pro Ala Gly Gly Ala His Leu Cys Ala Ala	
	100 105	
25	tggttggtga tggtggtgag cgtatccttc atggccagcg cgaagtcggc caggtcagcc	630
	aggctgtgc agcgcctctc ctcggacttg tcttcctgtg ccaggggacc gggagaaaag	690
	tgtcaggggc cgtcactgc agcagcctgc tctgtgcct tccttgcaag tgtctcggg	750
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	gagcttggga ccagggtctc tacacctaat tttctctcct ggtagctgaa caaaggctca	1170
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15  Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu Asp
      35             40             45
    Ser Val Thr Glu Ser Pro Gln Arg Val Ile Ile Thr Glu Asp Asp Glu
      50             55             60
    Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu Gly
20  65             70             75             80
    Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu Pro
      85             90             95
    Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr Ser
      100            105            110
25  Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala His
      115            120            125
    Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val Thr
      130            135            140
    Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys Asn
30  145            150            155            160
    Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu Glu
      165            170            175
    Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala Thr
      180            185            190
35  Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu Trp

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	195	200	205
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	Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg Pro		
5	225	230	235 240
	Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Glu Asp Met		
	245	250	255
	Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg Leu		
	260	265	270
10	Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro Lys		
	275	280	285
	Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser Glu		
	290	295	300
	Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His Phe		
15	305	310	315 320
	Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp Gln		
	325	330	335
	Phe Ser Gly Pro Lys Ile Met Gln Glu Glu Gly Gln Pro Leu Lys Leu		
	340	345	350
20	Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly Ser		
	355	360	365
	Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met Asn		
	370	375	380
	Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn Arg		
25	385	390	395 400
	Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu Asn		
	405	410	415
	Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser Arg		
	420	425	430
30	Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu Glu		
	435	440	445
	Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg Glu		
	450	455	460
	Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys Val		
35	465	470	475 480

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Lys Ala Met

<210> 122

<211> 334

5 <212> PRT

<213> Homo sapiens

<400> 122

10 Met Val Glu Phe Ala Pro Leu Phe Met Pro Trp Glu Arg Arg Leu Gln
 1 5 10 15
 Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala Leu Ala Glu
 20 25 30
 Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg Phe Trp Leu
 35 40 45
 15 Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg Asp Lys Pro
 50 55 60
 Arg Gln Gly Gly Arg His Ile Gln Ala Ile Arg Cys Trp Thr Ile Trp
 65 70 75 80
 Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys Thr Ala Glu
 20 85 90 95
 Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro His Gly Val
 100 105 110
 Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser Thr Gly Phe
 115 120 125
 25 Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met Leu Thr Leu
 130 135 140
 Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser Ala Gly Leu
 145 150 155 160
 Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn Arg Lys Gly
 30 165 170 175
 Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln Glu Ala Leu
 180 185 190
 Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn Arg Lys Gly
 195 200 205
 35 Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val Pro Ile Phe

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210 215 220
 Ser Phe Gly Glu Asn Asp Leu Phe Asp Gln Ile Pro Asn Ser Ser Gly
 225 230 235 240
 Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile Met Gly Ile
 5 245 250 255
 Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr Ser Phe Gly
 260 265 270
 Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly Lys Pro Ile
 275 280 285
 10 Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Glu Val Asn Gln Leu
 290 295 300
 His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu Ala His Lys
 305 310 315 320
 Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe Cys
 15 325 330

 <210> 123
 <211> 267
 <212> PRT
 20 <213> Homo sapience

 <400> 123
 Met Ala Pro Trp Ala Leu Leu Ser Pro Gly Val Leu Val Arg Thr Gly
 1 5 10 15
 25 His Thr Val Leu Thr Trp Gly Ile Thr Leu Val Leu Phe Leu His Asp
 20 25 30
 Thr Glu Leu Arg Gln Trp Glu Glu Gln Gly Glu Leu Leu Pro Leu
 35 40 45
 Thr Phe Leu Leu Leu Val Leu Gly Ser Leu Leu Leu Tyr Leu Ala Val
 30 50 55 60
 Ser Leu Met Asp Pro Gly Tyr Val Asn Val Gln Pro Gln Pro Gln Glu
 65 70 75 80
 Glu Leu Lys Glu Glu Gln Thr Ala Met Val Pro Pro Ala Ile Pro Leu
 85 90 95
 35 Arg Arg Cys Arg Tyr Cys Leu Val Leu Gln Pro Leu Arg Ala Arg His

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100 105 110
 Cys Arg Glu Cys Arg Arg Cys Val Arg Arg Tyr Asp His His Cys Pro
 115 120 125
 Trp Met Glu Asn Cys Val Gly Glu Arg Asn His Pro Leu Phe Val Val
 5 130 135 140
 Tyr Leu Ala Leu Gln Leu Val Val Leu Leu Trp Gly Leu Tyr Leu Ala
 145 150 155 160
 Trp Ser Gly Leu Arg Phe Phe Gln Pro Trp Gly Leu Trp Leu Arg Ser
 165 170 175
 10 Ser Gly Leu Leu Phe Ala Thr Phe Leu Leu Leu Ser Leu Phe Ser Leu
 180 185 190
 Val Ala Ser Leu Leu Leu Val Ser His Leu Tyr Leu Val Ala Ser Asn
 195 200 205
 Thr Thr Thr Trp Glu Phe Ile Ser Ser His Arg Ile Ala Tyr Leu Arg
 15 210 215 220
 Gln Arg Pro Ser Asn Pro Phe Asp Arg Gly Leu Thr Arg Asn Leu Ala
 225 230 235 240
 His Phe Phe Cys Gly Trp Pro Ser Gly Ser Trp Glu Thr Leu Trp Ala
 245 250 255
 20 Glu Glu Glu Glu Glu Gly Ser Ser Pro Ala Val
 260 265

 <210> 124
 <211> 106
 25 <212> PRT
 <213> Homo sapience

 <400> 124
 Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro Asn Lys Val Leu
 30 1 5 10 15
 Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala Leu Asp Asp Pro
 20 25 30
 Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly
 35 40 45
 35 Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser

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50 55 60
 Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp Thr Lys Gln Met
 65 70 75 80
 Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val Met Ser Tyr Leu
 5 85 90 95
 Gln Asn Pro Gln Pro Met Thr Pro Pro Trp
 100 105

 <210> 125
 10 <211> 224
 <212> PRT
 <213> Homo sapience

 <400> 125
 15 Met Thr Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro
 1 5 10 15
 Tyr Phe Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe
 20 25 30
 Trp Lys Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys
 20 35 40 45
 Lys Met Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Gly Ile
 50 55 60
 Tyr Asp Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp
 65 70 75 80
 25 Leu Ile Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu
 85 90 95
 Tyr Lys Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile
 100 105 110
 Met Ser Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe
 30 115 120 125
 Asp Trp Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val
 130 135 140
 His Tyr Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp
 145 150 155 160
 35 Leu Tyr His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser

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165 170 175
 Val Tyr Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu
 180 185 190
 Gly Ser Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu
 5 195 200 205
 Ala Leu Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser
 210 215 220

 <210> 126
 10 <211> 258
 <212> PRT
 <213> Homo sapiens

 <400> 126
 15 Met Ala Val Leu Ala Pro Leu Ile Ala Leu Val Tyr Ser Val Pro Arg
 1 5 10 15
 Leu Ser Arg Trp Leu Ala Gln Pro Tyr Tyr Leu Leu Ser Ala Leu Leu
 20 25 30
 Ser Ala Ala Phe Leu Leu Val Arg Lys Leu Pro Pro Leu Cys His Gly
 20 35 40 45
 Leu Pro Thr Gln Arg Glu Asp Gly Asn Pro Cys Asp Phe Asp Trp Arg
 50 55 60
 Glu Val Glu Ile Leu Met Phe Leu Ser Ala Ile Val Met Met Lys Asn
 65 70 75 80
 25 Arg Arg Ser Met Phe Leu Met Thr Cys Lys Pro Pro Leu Tyr Met Gly
 85 90 95
 Pro Glu Tyr Ile Lys Tyr Phe Asn Asp Lys Thr Ile Asp Glu Glu Leu
 100 105 110
 Glu Arg Asp Lys Arg Val Thr Trp Ile Val Glu Phe Phe Ala Asn Trp
 30 115 120 125
 Ser Asn Asp Cys Gln Ser Phe Ala Pro Ile Tyr Ala Asp Leu Ser Leu
 130 135 140
 Lys Tyr Asn Cys Thr Gly Leu Asn Phe Gly Lys Val Asp Val Gly Arg
 145 150 155 160
 35 Tyr Thr Asp Val Ser Thr Arg Tyr Lys Val Ser Thr Ser Pro Leu Thr

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165 170 175
 Lys Gln Leu Pro Thr Leu Ile Leu Phe Gln Gly Gly Lys Glu Ala Met
 180 185 190
 Arg Arg Pro Gln Ile Asp Lys Lys Gly Arg Ala Val Ser Trp Thr Phe
 5 195 200 205
 Ser Glu Glu Asn Val Ile Arg Glu Phe Asn Leu Asn Glu Leu Tyr Gln
 210 215 220
 Arg Ala Lys Lys Leu Ser Lys Ala Gly Asp Asn Ile Pro Glu Glu Gln
 225 230 235 240
 10 Pro Val Ala Ser Thr Pro Thr Thr Val Ser Asp Gly Glu Asn Lys Lys
 245 250 255
 Asp Lys

 <210> 127
 15 <211> 110
 <212> PRT
 <213> Homo sapience

 <400> 127
 20 Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro Pro Phe Ile Ser Glu
 1 5 10 15
 Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp Tyr Cys Arg Thr Ser
 20 25 30
 Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile Leu Gly Leu Thr Gly
 25 35 40 45
 Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser Val Leu Leu Ser Leu
 50 55 60
 Leu Leu Ile Leu Lys Ala Gly Arg Arg Trp Asn Lys Tyr Phe Lys Ser
 65 70 75 80
 30 Arg Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly Gly Leu Phe Thr Tyr
 85 90 95
 Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val His Val Tyr
 100 105 110

 35 <210> 128

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<211> 91

<212> PRT

<213> Homo sapiens

5 <400> 128

Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser Gln Ser
 1 5 10 15
 Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile Ala Glu
 20 25 30
 Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val Lys Lys
 35 40 45
 Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp Gly Arg
 50 55 60
 Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn His Leu
 65 70 75 80
 Arg Gly Pro Ser Pro Pro Pro Met Ala Gly Gly
 85 90

<210> 129

20 <211> 344

<212> PRT

<213> Homo sapiens

<400> 129

25 Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser
 1 5 10 15
 Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Ala Leu
 20 25 30
 Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val
 35 40 45
 Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys
 50 55 60
 Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Ile Tyr Asn Phe
 65 70 75 80
 35 Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu

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	85	90	95
	Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Glu		
	100	105	110
	Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser		
5	115	120	125
	Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser		
	130	135	140
	Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr		
	145	150	155
10	Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly		
	165	170	175
	Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys		
	180	185	190
	Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser		
15	195	200	205
	Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser		
	210	215	220
	Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp		
	225	230	235
20	Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe		
	245	250	255
	Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gln Gly Gly Met		
	260	265	270
	Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val		
25	275	280	285
	Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu		
	290	295	300
	Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg		
	305	310	315
30	Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val		
	325	330	335
	Ala Thr Asn Phe Leu Leu Gln His		
	340		
35	<210> 130		

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<211> 428

<212> PRT

<213> Homo sapiens

5 <400> 130

Met Gly Pro Pro Pro Gly Ala Gly Val Ser Cys Arg Gly Gly Cys Gly

1 5 10 15

Phe Ser Arg Leu Leu Ala Trp Cys Phe Leu Leu Ala Leu Ser Pro Gln

20 25 30

10 Ala Pro Gly Ser Arg Gly Ala Glu Ala Val Trp Thr Ala Tyr Leu Asn

35 40 45

Val Ser Trp Arg Val Pro His Thr Gly Val Asn Arg Thr Val Trp Glu

50 55 60

Leu Ser Glu Glu Gly Val Tyr Gly Gln Asp Ser Pro Leu Glu Pro Val

15 65 70 75 80

Ala Gly Val Leu Val Pro Pro Asp Gly Pro Gly Ala Leu Asn Ala Cys

85 90 95

Asn Pro His Thr Asn Phe Thr Val Pro Thr Val Trp Gly Ser Thr Val

100 105 110

20 Gln Val Ser Trp Leu Ala Leu Ile Gln Arg Gly Gly Gly Cys Thr Phe

115 120 125

Ala Asp Lys Ile His Leu Ala Tyr Glu Arg Gly Ala Ser Gly Ala Val

130 135 140

Ile Phe Asn Phe Pro Gly Thr Arg Asn Glu Val Ile Pro Met Ser His

25 145 150 155 160

Pro Gly Ala Val Asp Ile Val Ala Ile Met Ile Gly Asn Leu Lys Gly

165 170 175

Thr Lys Ile Leu Gln Ser Ile Gln Arg Gly Ile Gln Val Thr Met Val

180 185 190

30 Ile Glu Val Gly Lys Lys His Gly Pro Trp Val Asn His Tyr Ser Ile

195 200 205

Phe Phe Val Ser Val Ser Phe Phe Ile Ile Thr Ala Ala Thr Val Gly

210 215 220

Tyr Phe Ile Phe Tyr Ser Ala Arg Arg Leu Arg Asn Ala Arg Ala Gln

35 225 230 235 240

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Ser Arg Lys Gln Arg Gln Leu Lys Ala Asp Ala Lys Lys Ala Ile Gly
 245 250 255
 Arg Leu Gln Leu Arg Thr Leu Lys Gln Gly Asp Lys Glu Ile Gly Pro
 260 265 270
 5 Asp Gly Asp Ser Cys Ala Val Cys Ile Glu Leu Tyr Lys Pro Asn Asp
 275 280 285
 Leu Val Arg Ile Leu Thr Cys Asn His Ile Phe His Lys Thr Cys Val
 290 295 300
 Asp Pro Trp Leu Leu Glu His Arg Thr Cys Pro Met Cys Lys Cys Asp
 10 305 310 315 320
 Ile Leu Lys Ala Leu Gly Ile Glu Val Asp Val Glu Asp Gly Ser Val
 325 330 335
 Ser Leu Gln Val Pro Val Ser Asn Glu Ile Ser Asn Ser Ala Ser Ser
 340 345 350
 15 His Glu Glu Asp Asn Arg Ser Glu Thr Ala Ser Ser Gly Tyr Ala Ser
 355 360 365
 Val Gln Gly Thr Asp Glu Pro Pro Leu Glu Glu His Val Gln Ser Thr
 370 375 380
 Asn Glu Ser Leu Gln Leu Val Asn His Glu Ala Asn Ser Val Ala Val
 20 385 390 395 400
 Asp Val Ile Pro His Val Asp Asn Pro Thr Phe Glu Glu Asp Glu Thr
 405 410 415
 Pro Asn Gln Glu Thr Ala Val Arg Glu Ile Lys Ser
 420 425
 25
 <210> 131
 <211> 1449
 <212> DNA
 <213> Homo sapience
 30
 <400> 131
 atgaagcct tccacacttt ctgtgttgct cttctggtgt ttgggagtgt ctctgaagcc 60
 aagtttgatg attttgagga tgaggaggac atagtagagt atgatgataa tgacttcgct 120
 gaatttgagg atgtcatgga agactctggt actgaatctc ctcaacgggt cataatcact 180
 35 gaagatgatg aagatgagac cactgtggag ttggaagggc aggatgaaa ccaagaagga 240

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	gattttgaag atgcagatac ccaggaggga gatactgaga gtgaaccata tgatgatgaa	300
	gaattttgaag gttatgaaga caaaccagat actcttctta gcaaaaataa agaccaata	360
	acgattgttg atgttcctgc acacctccag aacagctggg agagtattta totagaaatt	420
	ttgatgggtga ctggtctgct tgottatatac atgaattaca tcattgggaa gaataaaaaac	480
5	agtcgccttg cacaggcctg gtttaacact cataggggagc ttttggagag caactttact	540
	ttagtggggg atgatggaac taacaaagaa gccacaagca caggaaagt gaaccaggag	600
	aatgagcaca tctataacct gtggtgttct ggtcgagtgt gctgtgaggg catgottatc	660
	cagctgaggt tctcaagag acaagactta ctgaatgtcc tggcccgat gatgaggcca	720
	gtgagtgtac aagtgcaaat aaaagtaacc atgaatgatg aagacatgga tacctacgta	780
10	tttctgtgtg gcacacggaa agccttggtg cgactacaga aagagatgca ggatttgagt	840
	gagttttgta gtgataaacc taagtctgga gcaaatgatg gactgccgga ctctttggcc	900
	atcctgtcag agatgggaga agtcacagac ggaatgatgg atacaaagat ggttcaactt	960
	cttacacact atgtcgacaa gattgaatct gttcattttt cagaccagt ctctggtcca	1020
	aaaattatgc aagaggaagg tcagccttta aagctacctg acactaagag gacactgttg	1080
15	tttacattta atgtgcctgg ctacagtaac acttacccaa aggatattgga ggcactgcta	1140
	ccctgatga acatggtgat ttattctatt gataaagcca aaaagtccc actcaacaga	1200
	gaaggcacaac aaaaagcaga taagaaccgt gcccgagtag aagagaactt cttgaaactg	1260
	acacatgtgc aaagacagga agcagcacag tctcgccggg aggagaaaaa aagagcagag	1320
	aaggagcgaa tcatgaatga ggaagatcct gagaacacgc gcaggctgga ggaggctgca	1380
20	ttgaggctg agcaaaagaa gttggaaaag aagcaaatga aaatgaaca aatcaaaagt	1440
	aaagccatg	1449
	<210> 132	
	<211> 1002	
25	<212> DNA	
	<213> Homo sapience	
	<400> 132	
	atggtagagt tcgcgcctt gtttatgccg tgggagcgca ggctgcagac acttgctgtc	60
30	ctacagtttg tottctcctt cttggcaactg gccagagatct gcaactgtggg cttoatagcc	120
	ctcctgttta caagattctg gctcctcact gtctgtgatg cggcctggtg gtatctggac	180
	cgagacaagc cacggcaggg gggccggcac atccaggcca tcaggtgctg gactatatgg	240
	aagtacatga aggactattt ccccatctcg ctggtoaaga ctgctgagct ggacccctct	300
	cggactaca ttgcgggett ccaccccat ggagtctcgg cagtcggagc ctttgccaa	360
35	ctgtgcaactg agagcacagg cttctcttcg atcttcccgc gtatccgccc ccatctgatg	420

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atgtgtgacct tgtggttccg ggcccccttc ttcagagatt acatcatgtc tgcagggttg 480
 gtcacatcag aaaaggagag tgcgtgtcac attctgaaca ggaagggttg cggaaacttg 540
 ctgggcatca ttgtaggggg tgcacaggag gccctggatg ccaggcctgg atccttcacg 600
 ctgttactgc ggaaccgaaa gggtctcgtc aggctcgccc tgacacacgg ggcaccctcg 660
 5 gtgccaatct tctccttcgg ggagaatgac ctatttgacc agattcccaa ctcttctggc 720
 tctcggttac gctatatcca gaatcggttg cagaagatca tgggcacttc cctcccaactc 780
 tttcatggcc gtggtgtctt ccagtacagc tttggtttaa taacctacgg ccggcccatc 840
 accactgtgg tggggaagcc catcgaggta cagaagacgc tgcctccctc ggaggaggag 900
 gtgaaccagc tgcaccagcg ttatatcaaa gagctgtgca acctcttcga ggcccaacaa 960
 10 cttaagtcca acatccctgc tgaccagcac ttggagtctc gc 1002

<210> 133

<211> 801

<212> DNA

15 <213> Homo sapiens

<400> 133

atggcgccct gggcgtcct cagccctggg gtctgtgtgc ggaccgggca caccgtgtgtg 60
 acctggggaa tcacgttgtt gctcttctcg cagcataccg agctgcggca atgggaggag 120
 20 cagggggagc tgcctctgcc cctcaccttc ctgctctctg tgcctgggtc cctgctgtgc 180
 tactctctgt tgcactcat ggacctggc taagtgaatg tgcagcccca gcctcaggag 240
 gagctcaaa aggagcagac agccatggtt cctccagcca tccctctctg gcgtgcagga 300
 tactgctgtg tgcgcagcc cctgagggtt cggcactgcc gtgagtgcg ccgttgctgc 360
 cgcgcgtacg accaccactg cccctggatg gagaactgtg tgggagagcg caaccaccca 420
 25 ctcttttgtg tctactggc gctgcagctg gtggtgtctc tgtggggcct gtacctggca 480
 tggtagccgc tccggttctt ccagccctgg ggtctgtgtt tgcggtccag cgggtctctg 540
 ttgcgcacct tctgtgtgt gtcctctctc tctgtgtgtg ccagcctgct cctctgtctg 600
 caactctacc tgggtggcag caacacaccc acctgggaat tcatctctc acaccgcatc 660
 gcctatctcc gccagcgccc cagcaacccc ttgcacagag gctgacccg caacctggcc 720
 30 caattctctt gtggtatgcc ctacgggttc tgggagaccc tctgggctga ggaggaggaa 780
 gggggcagca gccacgtgt t 801

<210> 134

<211> 318

35 <212> DNA

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<213> Homo sapiens

<400> 134

5 atgtccaacta acaatatgtc ggaccacggy aggccgaaca aagtgtgtgag gtacaagccc 60
 ccgccgagcg aatgtaaccc ggcccttgag gaccggacgc cggactacat gaacctgtgt 120
 ggcgatgatc tcagcatgtg cggcctcatg ctttaagtga agtggtgtgc ttgggtcgtc 180
 gtctactgtc ccttcacag ctttgccaac tctcggagct cggaggacac gaagcaaatg 240
 atgagtagct tcattgtgtc catctctgcc gtggtgatgt cctatctgca gaactctcag 300
 cccatgacgc ccccatgg 318

10

<210> 135

<211> 672

<212> DNA

<213> Homo sapiens

15

<400> 135

atgacacctgt ttcaactcgg gaactgtctc gctcttgccct acttccccta cttcaccacc 60
 tacaagtga cgggcctgtc cgagtacaac gcctcttgga aatgcgtcca ggtcggagtc 120
 acctacctct ttgtccaaact ctgcaagatg ctgttcttg ccaatttctt tcccacctgg 180
 20 gaaggcggca tctatgaact cattggggag ttcattgaagg ccagcgtgga tgtggcagac 240
 ctgataggtc taaaccttgt catgtcccg aatgccggca agggagagta caagatcatg 300
 gttgtctgcc tgggctgggc caactgtgag cttattatgt cccgtgcat tcccctatgg 360
 gtcggagccc ggggcattga gtttgactgg aagtacatcc agatgagcat agactccaac 420
 atcagcttgg tccattacat cgtcgcgtct gctcaggtct ggatgataac acgctatgat 480
 25 ctgtaccaca ccttcggccc agctgtcctc ctgtgtatgt tctcagtggt ctacaaggcc 540
 ttgttatatg agaccttctg ccaactctgc tctgtgggca gttgggcage tctactggcc 600
 cgagcagtggt taacggggct gctggccctc agcaacttgg cctgtatgt cgcgctgtgc 660
 aatgtgcaact cc 672

30

<210> 136

<211> 774

<212> DNA

<213> Homo sapiens

35

<400> 136

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PCT/JP99/03929

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	atggcggtct tggcacetct aattgctctc gtgtattcgg tgccgcgact ttcacgatgg	60
	ctcgcccaac cttactacct tctgtggccc ctgctctctg ctgccttccct actcgtgagg	120
	aaactgcgc cgcctctgcc cggtctgccc acccaacgcg aagacggtaa cccgtgtgac	180
	tttgactgga gagaagtgga gatcctgatg tttctcagtg ccaattgtgat gatgaagaac	240
5	cgcagatcca tgttctctgat gacgtgcaaa cccccctat atattggccc tgagtatac	300
	aagtacttca atgataaaac cattgatgag gaactagaac gggacaagag ggtoacttgg	360
	attgtggagt tctttgccaa ttggtctaat gactgccaat catttgcctc tatctatgct	420
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	Ser	Val	Ser	Glu	Ala	Lys	Phe	Asp	Asp	Phe	Glu	Asp	Glu	Glu	Asp	Ile	
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	Val	Glu	Tyr	Asp	Asn	Asp	Phe	Ala	Glu	Phe	Glu	Asp	Val	Met	Glu		
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	gac	tct	gtt	act	gaa	tct	cct	caa	cgg	gtc	ata	atc	act	gaa	gat	gat	310
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	Glu	Asp	Glu	Thr	Thr	Val	Glu	Leu	Glu	Gly	Gln	Asp	Glu	Asn	Gln	Glu	
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	Gly	Asp	Phe	Glu	Asp	Ala	Asp	Thr	Gln	Glu	Gly	Asp	Thr	Glu	Ser	Glu	
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	Pro	Tyr	Asp	Asp	Glu	Glu	Phe	Glu	Gly	Tyr	Glu	Asp	Lys	Pro	Asp	Thr	
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	Ser	Ser	Ser	Lys	Asn	Lys	Asp	Pro	Ile	Thr	Ile	Val	Asp	Val	Pro	Ala	
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	Thr	Gly	Leu	Leu	Ala	Tyr	Ile	Met	Asn	Tyr	Ile	Ile	Gly	Lys	Asn	Lys	
						145					150				155		
30	aac	agt	cgc	ctt	gca	cag	gcc	tgg	ttt	aac	act	cat	agg	gag	ctt	ttg	646
	Asn	Ser	Arg	Leu	Ala	Gln	Ala	Trp	Phe	Asn	Thr	His	Arg	Glu	Leu	Leu	
						160					165				170		
	gag	agc	aac	ttt	act	tta	gtg	ggg	gat	gat	gga	act	aac	aaa	gaa	gcc	694
	Glu	Ser	Asn	Phe	Thr	Leu	Val	Gly	Asp	Asp	Gly	Thr	Asn	Lys	Glu	Ala	
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	ttc ctc aag aga caa gac tta ctg aat gtc ctg gcc cgg atg atg agg	838
	Phe Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg	
	225 230 235	
10	cca gtg agt gat caa gtg caa ata aaa gta acc atg aat gat gaa gac	886
	Pro Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Glu Asp	
	240 245 250 255	
	atg gat acc tac gta ttt gct gtt ggc aca cgg aaa gcc ttg gtg cga	934
	Met Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg	
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	cta cag aaa gag atg cag gat ttg agt gag ttt tgt agt gat aaa cct	982
	Leu Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro	
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20	Lys Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser	
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	Glu Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His	
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	Phe Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp	
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	cag ttc tct ggt cca aaa att atg caa gag gaa ggt cag cct tta aag	1174
	Gln Phe Ser Gly Pro Lys Ile Met Gln Glu Glu Gly Gln Pro Leu Lys	
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	Leu Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly	
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	tca ggt aac act tac cca aag gat atg gag gca ctg cta ccc ctg atg	1270
35	Ser Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met	

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	385	390	395	
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	Arg Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu			
	400	405	410	415
	aac ttc ttg aaa ctg aca cat gtg caa aga cag gaa gca gca cag tct			1414
	Asn Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser			
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	cgg cgg gag gag aaa aaa aga gca gag aag gag cga atc atg aat gag			1462
	Arg Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu			
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	gaa gat cct gag aaa cag cgc agg ctg gag gag gct gca ttg agg cgt			1510
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	gag caa aag aag ttg gaa aag aag caa atg aaa atg aaa caa atc aaa			1558
	Glu Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys			
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	Val Lys Ala Met			
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Met Val Glu Phe Ala Pro Leu Phe Met Pro Trp Glu Arg

1

5

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10 agg ctg cag aca ctt gct gtc cta cag ttt gtc ttc tcc ttc ttg gca 156

Arg Leu Gln Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala

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25

ctg gcc gag atc tgc act gtg ggc ttc ata gcc ctc ctg ttt aca aga 204

Leu Ala Glu Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg

15

30 35 40 45

ttc tgg ctc ctc act gtc ctg tat gcg gcc tgg tgg tat ctg gac cga 252

Phe Trp Leu Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg

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55

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20

65

70

75

act ata tgg aag tac atg aag gac tat ttc ccc atc tgc ctg gtc aag 348

Thr Ile Trp Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys

80

85

90

25 act gct gag ctg gac ccc tct cgg aac tac att gcg ggc ttc cac ccc 396

Thr Ala Glu Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro

95

100

105

cat gga gtc ctg gca gtc gga gcc ttt gcc aac ctg tgc act gag agc 444

His Gly Val Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser

30

110 115 120 125

aca ggc ttc tct tgc atc ttc ccc ggt atc cgc ccc cat ctg atg atg 492

Thr Gly Phe Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met

130

135

140

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35

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5	agg aag ggt ggc gga aac ttg ctg ggc atc att gta ggg ggt gcc cag			636
	Arg Lys Gly Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln			
	175	180	185	
	gag gcc ctg gat gcc agg cct gga tcc ttc acg ctg tta ctg cgg aac			684
	Glu Ala Leu Asp Ala Arg Pro Gly Ser Phe Thr Leu Leu Leu Arg Asn			
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	cga aag ggc ttc gtc agg ctc gcc ctg aca cac ggg gca ccc ctg gtg			732
	Arg Lys Gly Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val			
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	240	245	250	
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	Met Gly Ile Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr			
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	agc ttt ggt tta ata ccc tac cgc cgg ccc atc acc act gtg gtg ggg			924
	Ser Phe Gly Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly			
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30	Asn Gln Leu His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu			
	305	310	315	
	gcc cac aaa ctt aag ttc aac atc cct gct gac cag cac ttg gag ttc			1068
	Ala His Lys Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe			
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	Ser Pro Gly Val Leu Val Arg Thr Gly His Thr Val Leu Thr Trp Gly	
10	10 15 20	
	atc acg ctg gtg ctc ttc ctg cac gat acc gag ctg cgg caa tgg gag	148
	Ile Thr Leu Val Leu Phe Leu His Asp Thr Glu Leu Arg Gln Trp Glu	
	25 30 35	
	gag cag ggg gag ctg ctc ctg ccc ctc acc ttc ctg ctc ctg gtg ctg	196
15	Glu Gln Gly Glu Leu Leu Leu Pro Leu Thr Phe Leu Leu Leu Val Leu	
	40 45 50 55	
	ggc tcc ctg ctg ctc tac ctc gct gtg tca ctc atg gac cct ggc tac	244
	Gly Ser Leu Leu Leu Tyr Leu Ala Val Ser Leu Met Asp Pro Gly Tyr	
	60 65 70	
20	gtg aat gtg cag ccc cag cct cag gag gag ctc aaa gag gag cag aca	292
	Val Asn Val Gln Pro Gln Pro Gln Glu Leu Lys Glu Glu Gln Thr	
	75 80 85	
	gcc atg gtt cct cca gcc atc cct ett cgg cgc tgc aga tac tgc ctg	340
	Ala Met Val Pro Pro Ala Ile Pro Leu Arg Arg Cys Arg Tyr Cys Leu	
25	90 95 100	
	gtg ctg cag ccc ctg agg gct cgg cac tgc cgt gag tgc cgc cgt tgc	388
	Val Leu Gln Pro Leu Arg Ala Arg His Cys Arg Glu Cys Arg Arg Cys	
	105 110 115	
	gtc cgc cgc tac gac cac cac tgc ccc tgg atg gag aac tgt gtg gga	436
30	Val Arg Arg Tyr Asp His His Cys Pro Trp Met Glu Asn Cys Val Gly	
	120 125 130 135	
	gag cgc aac cac cca ctc ttt gtg gtc tac ctg gcg ctg cag ctg gtg	484
	Glu Arg Asn His Pro Leu Phe Val Val Tyr Leu Ala Leu Gln Leu Val	
	140 145 150	
35	gtg ctt ctg tgg ggc ctg tac ctg gca tgg tca ggc ctc cgg ttc ttc	532

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Val Leu Leu Trp Gly Leu Tyr Leu Ala Trp Ser Gly Leu Arg Phe Phe
155 160 165
cag ccc tgg ggt ctg tgg ttg cgg tcc agc ggg ctc ctg ttc gcc acc 580
Gln Pro Trp Gly Leu Trp Leu Arg Ser Ser Gly Leu Leu Phe Ala Thr
5 170 175 180
ttc ctg ctg ctg tcc ctc ttc tgg ttg gtg gcc agc ctg ctc ctc gtc 628
Phe Leu Leu Leu Ser Leu Phe Ser Leu Val Ala Ser Leu Leu Leu Val
185 190 195
tcg cac ctc tac ctg gtg gcc agc aac acc acc acc tgg gaa ttc atc 676
10 Ser His Leu Tyr Leu Val Ala Ser Asn Thr Thr Thr Trp Glu Phe Ile
200 205 210 215
tcc tca cac cgc atc gcc tat ctc cgc cag cgc ccc agc aac ccc ttc 724
Ser Ser His Arg Ile Ala Tyr Leu Arg Gln Arg Pro Ser Asn Pro Phe
220 225 230
15 gac cga ggc ctg acc cgc aac ctg gcc cac ttc ttc tgt gga tgg ccc 772
Asp Arg Gly Leu Thr Arg Asn Leu Ala His Phe Phe Cys Gly Trp Pro
235 240 245
tca ggg tcc tgg gag acc ctc tgg gct gag gag gag gaa gag ggc agc 820
Ser Gly Ser Trp Glu Thr Leu Trp Ala Glu Glu Glu Glu Glu Gly Ser
20 250 255 260
agc cca gct gtt taggggtgct ggaggecggy ctaccgtctt gtgectga 870
Ser Pro Ala Val
265
aaaccacggg gctgtcccc agctgggggtg agcgcctcaga gggcctgggg ccctcactcc 930
25 tgcccacgcc tcccagaccc cagaacggag ctccaagtca gacagatccc tgccctgggtg 990
ggcagttctg cttccaagg aagaaggga agaaaaggac ctgtgggttg ctcaggccca 1050
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<213> Homo sapience
<220>
35 <221> CDS

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<222> (13)...(333)

<400> 144

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	1 5 10	
	aac aaa gtg ctg agg tac aag ccc cgg cgg agc gaa tgt aac cgg gcc	96
	Asn Lys Val Leu Arg Tyr Lys Pro Pro Ser Glu Cys Asn Pro Ala	
	15 20 25	
10	ttg gac gac cgg acg cgg gac tac atg aac ctg ctg ggc atg atc ttc	144
	Leu Asp Asp Pro Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe	
	30 35 40	
	agc atg tgc ggc ctc atg ctt aag ctg aag tgg tgt gct tgg gtc gct	192
	Ser Met Cys Gly Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala	
15	45 50 55 60	
	gtc tac tgc tcc ttc atc agc ttt gcc aac tct cgg agc tcg gag gac	240
	Val Tyr Cys Ser Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp	
	65 70 75	
	acg aag caa atg atg agt agc ttc atg ctg tcc atc tct gcc gtg gtg	288
20	Thr Lys Gln Met Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val	
	80 85 90	
	atg tcc tat ctg cag aat cct cag ccc atg acg ccc cca tgg	340
	Met Ser Tyr Leu Gln Asn Pro Gln Pro Met Thr Pro Pro Trp	
	95 100 105	
25	tgataccagc ctagaagggt cacattttgg acctgtcta tccactagc ctgggctttg	390
	gtcgtctaaac ctgtgcctt cagctgccat cctggaactc cctgaatgag gccgtctcgg	450
	tgccccacagc tggatagagg gaacctggcc ctttctagg gaacacctca ggcttacccc	510
	tctgcctccc cttcccctgc ctgctgctgg gggagatgct gtccatgttt ctagggggtat	570
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					Met Thr		
					1		
	ctg ttt cac ttc ggg aac tgc ttc gct ctt gcc tac ttc ccc tac ttc						164
10	Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro Tyr Phe						
	5	10	15				
	atc acc tac aag tgc agc gcc ctg tcc gag tac aac gcc ttc tgg aaa						212
	Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe Trp Lys						
	20	25	30				
15	tgc gtc cag gct gga gtc acc tac ctc ttt gtc caa ctc tgc aag atg						260
	Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys Lys Met						
	35	40	45	50			
	ctg ttc ttg gcc act ttc ttt ccc acc tgg gaa gcc gcc atc tat gac						308
	Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Gly Ile Tyr Asp						
20		55	60	65			
	ttc att ggg gag ttc atg aag gcc agc gtg gat gtg gca gac ctg ata						356
	Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp Leu Ile						
	70	75	80				
	ggg cta aac ctt gtc atg tcc cgg aat gcc gcc aag gga gag tac aag						404
25	Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu Tyr Lys						
	85	90	95				
	atc atg gtt gct gcc ctg gcc tgg gcc act gct gag ctt att atg tcc						452
	Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile Met Ser						
	100	105	110				
30	cgc tgc att ccc cta tgg gtc gga gcc cgg gcc att gag ttt gac tgg						500
	Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe Asp Trp						
	115	120	125	130			
	aag tac atc cag atg agc ata gac tcc aac atc agt ctg gtc cat tac						548
	Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val His Tyr						
35		135	140	145			

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atc gtc gcg tct gct cag gtc tgg atg ata aca cgc tat gat ctg tac 596
 Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp Leu Tyr
 150 155 160
 cac acc ttc cgg cca gct gtc ctc ctg ctg atg ttc ctc agt gtc tac 644
 5 His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser Val Tyr
 165 170 175
 aag gcc ttt gtt atg gag acc ttc gtc cac ctc tgc tcg ctg ggc agt 692
 Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu Gly Ser
 180 185 190
 10 tgg gca gct cta ctg gcc cga gca gtg gta acg ggg ctg ctg gcc ctc 740
 Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu Ala Leu
 195 200 205 210
 agc act ttg gcc ctg tat gtc gcc gtt gtc aat gtg cac tcc taggcttg 790
 Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser
 15 215 220
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 gtatttgga agtt 864
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 20 <211> 1527
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 25 <222> (25)...(801)
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 Met Ala Val Leu Ala Pro Leu Ile Ala
 30 1 5
 ctc gtg tat tcg gtg ccg cga ctt tca cga tgg ctc gcc caa cct tac 99
 Leu Val Tyr Ser Val Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr
 10 15 20 25
 tac ctt ctg tcg gcc ctg ctc tct gct gcc ttc cta ctc gtg agg aaa 147
 35 Tyr Leu Leu Ser Ala Leu Leu Ser Ala Ala Phe Leu Leu Val Arg Lys

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	30	35	40	
	ctg ccg ccg ctc tgc cac ggt ctg ccc acc caa cgc gaa gac ggt aac			195
	Leu Pro Pro Leu Cys His Gly Leu Pro Thr Gln Arg Glu Asp Gly Asn			
	45	50	55	
5	ccg tgt gac ttt gac tgg aga gaa gtg gag atc ctg atg ttt ctc agt			243
	Pro Cys Asp Phe Asp Trp Arg Glu Val Glu Ile Leu Met Phe Leu Ser			
	60	65	70	
	gcc att gtg atg atg aag aac cgc aga tcc atg ttc ctg atg acg tgc			291
	Ala Ile Val Met Met Lys Asn Arg Arg Ser Met Phe Leu Met Thr Cys			
10	75	80	85	
	aaa ccc ccc cta tat atg ggc cct gag tat atc aag tac ttc aat gat			339
	Lys Pro Pro Leu Tyr Met Gly Pro Glu Tyr Ile Lys Tyr Phe Asn Asp			
	90	95	100	105
	aaa acc att gat gag gaa cta gaa cgg gac aag agg gtc act tgg att			387
15	Lys Thr Ile Asp Glu Leu Glu Arg Asp Lys Arg Val Thr Trp Ile			
	110	115	120	
	gtg gag ttc ttt gcc aat tgg tct aat gac tgc caa tca ttt gcc cct			435
	Val Glu Phe Phe Ala Asn Trp Ser Asn Asp Cys Gln Ser Phe Ala Pro			
	125	130	135	
20	atc tat gct gac ctc tcc ctt aaa tac aac tgt aca ggg cta aat ttt			483
	Ile Tyr Ala Asp Leu Ser Leu Lys Tyr Asn Cys Thr Gly Leu Asn Phe			
	140	145	150	
	ggg aag gtg gat gtt gga cgc tat act gat gtt agt acg cgg tac aaa			531
	Gly Lys Val Asp Val Gly Arg Tyr Thr Asp Val Ser Thr Arg Tyr Lys			
25	155	160	165	
	gtg agc aca tca ccc ctc acc aag caa ctc cct acc ctg atc ctg ttc			579
	Val Ser Thr Ser Pro Leu Thr Lys Gln Leu Pro Thr Leu Ile Leu Phe			
	170	175	180	185
	caa ggt ggc aag gag gca atg cgg cgg cca cag att gac aag aaa gga			627
30	Gln Gly Gly Lys Glu Ala Met Arg Arg Pro Gln Ile Asp Lys Lys Gly			
	190	195	200	
	cgg gct gtc tca tgg acc ttc tct gag gag aat gtg atc cga gaa ttt			675
	Arg Ala Val Ser Trp Thr Phe Ser Glu Glu Asn Val Ile Arg Glu Phe			
	205	210	215	
35	aac tta aat gag cta tac cag cgg gcc aag aaa cta tca aag gct gga			723

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Asn Leu Asn Glu Leu Tyr Gln Arg Ala Lys Lys Leu Ser Lys Ala Gly
 220 225 230
 gac aat atc cct gag gag cag cct gtg gct tca acc ccc acc aca gtg 771
 Asp Asn Ile Pro Glu Glu Gln Pro Val Ala Ser Thr Pro Thr Thr Val
 5 235 240 245
 tca gat ggg gaa aac aag aag gat aaa taagatcctc ac 810
 Ser Asp Gly Glu Asn Lys Lys Asp Lys
 250 255
 tttggcagtg ctctctctcc tgtcaattcc aggctctttc cataaccaca agcctgaggc 870
 10 tgcagccctt tatttatgtt ttccctttgg ctgtgactgg gtggggcagc atgcagcttc 930
 tgcattttaaa gaggcatac ggggaattgtc aggcacccta caggaaggcc tgcctagctg 990
 tggccaaactg ttctactgga gcaagaaaga gatctcatag gacggagggg gaaatggttt 1050
 cctcccaage ttgggtcagt gtgttaactg cttatcagct attcagacat ctccatgggt 1110
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 15 acctagattt aaccctaagg taagatgctg ggtatagaa cgctaagaat ttcccccaa 1230
 ggactcttgc ttccctaagc cctcttggtc tegtcttagg tottcattaa aagtataage 1290
 ctaactttgt cgctagtctt aaggagaaac ctttaaccac aaagttttta tcattgaaga 1350
 caatattgaa caacccccca ttttgtgggg attgagaagg ggtgaataga ggcttgagac 1410
 ttctctttgt gtggtaggac ttggaggaga aatccctgg accttacta accctctgac 1470
 20 atactcccca caccagttg atggtcttcc gtaataaaaa gattgggatt tctcttt 1527

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 aagtagtgty tccggcgccg tgttccagct ccgcgttggt ccgcgagaaa gcgagaggcc 120
 gagcccgccc tgggtgcy atg gcc gcg gty gty gcc aag cgg gaa ggg cgg 170
 Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro
 35 1 5 10

	ccg ttc atc agc agc gag gcg gcc gtc ggc ggc aac gcc gcc gtc gat	218
	Pro Phe Ile Ser Glu Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp	
	15 20 25	
5	tat tgc cgg acc tcg gtc tca gcg ctg tcg ggg gcc acg gcc ggc atc	266
	Tyr Cys Arg Thr Ser Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile	
	30 35 40	
	ctc gcc ctc acc gcc ctc tac gcc ttc atc ttc tac ctg ctc gcc tcc	314
	Leu Gly Leu Thr Gly Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser	
	45 50 55	
10	gtc ctg ctc tcc ctg ctc ctc att ctc aag gcg gga agg agg tgg aac	362
	Val Leu Leu Ser Leu Leu Leu Ile Leu Lys Ala Gly Arg Arg Trp Asn	
	60 65 70 75	
	aaa tat ttc aaa tca cgg aga cct ctc ttt aca gga gcc ctc atc ggg	410
	Lys Tyr Phe Lys Ser Arg Arg Pro Leu Phe Thr Gly Gly Leu Ile Gly	
15	80 85 90	
	ggc ctc ttc acc tac gtc ctg ttc tgg acg ttc ctc tac gcc atg gtc	458
	Gly Leu Phe Thr Tyr Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val	
	95 100 105	
	cac gtc tac tgaatatggg gcccgggga cttttttaa aaa	500
20	His Val Tyr	
	110	
	ccagatcggg aggactgtgg ccagcaatta acaccatgta gacttcctta gttcttaagt	560
	ggttgaattc gctgcttgtt ctgtaacggt ataaataatt tatatctgaa gacggagagc	620
	ctgtaatat cttcagatta aatgaagcgt gagacactt	659
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ggacaag atg gtt tac atc tcg aac gga caa gtg ttg gac agc cgg agt 109
 Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser
 1 5 10
 cag tct cca tgg aga tta tct ttg ata aca gat ttc ttc tgg gga ata 157
 5 Gln Ser Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile
 15 20 25 30
 gct gag ttt gtg gtt ttg ttt ttc aaa act ctg ctt cag caa gat gtg 205
 Ala Glu Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val
 35 40 45
 10 aaa aaa aga aga agc tat gga aac tca tct gat tcc aga tat gat gat 253
 Lys Lys Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp
 50 55 60
 gga aga ggg cca cca gga aac cct ccc cga aga atg ggt aga atc aat 301
 Gly Arg Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn
 15 65 70 75
 cat ctg cgt ggc cct agt ccc cct cca atg gct ggt gga tgaggaaggt 350
 His Leu Arg Gly Pro Ser Pro Pro Pro Met Ala Gly Gly
 80 85 90
 aaatgtctgc tctaagaagc agacaaccgg acatgcgcac tcatagcaga aggaaccat 410
 20 caagaagtgg aaggctgacc atgatgagca gtagatgaat gtgtatgtct aaacaaggac 470
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 cctgactgac atgcagtcc ataaatgcag atgtttgtct cattaccttt ttgtatagtt 590
 tattaagta ttaatatagt ttaataagt aaatatTTTT aggttcgaga atggactcct 650
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 25
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 30 <220>
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 35 gcacttcagc ttcccctccc ccggcgccct ctggggctcc gagcccgag ggacc 58

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	atg ttc acc agc acc ggc tcc agt ggg ctc tac aag gcg cct ctg tgg	103
	Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser	
	1 5 10 15	
	aag agc ctt ctg ctg gtc ccc agt gcc ctc tcc ctc ctg ctc gcc ctc	151
5	Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu	
	20 25 30	
	ctc ctg cct cac tgc cag aag ctc ttt gtg tat gac ctt cac gca gtc	199
	Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val	
	35 40 45	
10	aag aac gac ttc cag att tgg agg ttg ata tgt gga aga ata att tgc	247
	Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys	
	50 55 60	
	ctt gat ttg aaa gat act ttc tgc agt agt ctg ctt att tat aat ttt	295
	Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe	
15	65 70 75 80	
	agg ata ttt gaa aga aga tat gga agc aga aaa ttt gca tcc ttt ttg	343
	Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu	
	85 90 95	
	ctg ggt tcc tgg gtt ttg tca gcc tta ttt gac ttt ctc ctc att gaa	391
20	Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Glu	
	100 105 110	
	gct atg cag tat ttc ttt ggc atc act gca gct agt aat ttg cct tct	439
	Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser	
	115 120 125	
25	gga ttc ctg gca cct gtg ttt gct ctg ttt gta cca ttt tac tgc tcc	487
	Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser	
	130 135 140	
	ata cca aga gtc caa gtg gca caa att ctg ggt ccg ttg tcc atc aca	535
	Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr	
30	145 150 155 160	
	aac aag aca ttg att tat ata ttg gga ctg cag ctt ttc acc tct ggt	583
	Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly	
	165 170 175	
	tcc tac atc tgg att gta gcc ata agt gga ctt atg tcc ggt ctg tgc	631
35	Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys	

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	180	185	190	
	tac gac agc aaa atg ttc cag gtg cat cag gtg ctc tgc atc ccc agc	679		
	Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser			
	195	200	205	
5	tgg atg gca aaa ttc ttt tct tgg aca ctt gaa ccc atc ttc tct tct	727		
	Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser			
	210	215	220	
	tca gaa ccc acc agc gaa gcc aga att ggg atg gga gcc acg ctg gac	775		
	Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp			
10	225	230	235	240
	atc cag aga cag cag aga atg gag ctg ctg gac cgg cag ctg atg ttc	823		
	Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe			
	245	250	255	
	tct cag ttt gca caa ggg agg cga cag aga cag cag gga gga atg	871		
15	Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gly Gly Met			
	260	265	270	
	atc aat tgg aat cgt ctt ttt cct cct tta cgt cag cga caa aac gta	919		
	Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val			
	275	280	285	
20	aac tat cag ggc ggt cgg cag tct gag cca gca gcg ccc cct cta gaa	967		
	Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu			
	290	295	300	
	gtt tct gag gaa cag gtc gcc cgg ctc atg gag atg gga ttt tcc aga	1015		
	Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg			
25	305	310	315	320
	ggc gat gct ttg gaa gcc ctg aga gct tca aac aat gac ctc aat gtc	1063		
	Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val			
	325	330	335	
	gcc aac aac ttc ctg ctg cag cac tgatagtcac aggccaaac tgg	1110		
30	Ala Thr Asn Phe Leu Leu Gln His			
	340			
	gaccggaccg gcagccaggt gacagtgcgt ggtccccacc atcagatcag cccggggacc	1170		
	gagcatctct ggtgctgatg ttcttgtggg aagagggagg ttccaacgca cccctgccct	1230		
	caaccgcaag actgttgccg ttttagtggt gagataagtt tgccattaca ttagcatgta	1290		
35	ttttctatct atatttttta ttgggcattt tcacctagggt ggagagtcag cactcgtttt	1350		

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	agggtaatgt	tacttcacaa	aggacatgtc	agatccttct	tcatggactt	ttttagttaac	1530
	tgttttttct	ctcaaaacttg	ttttcgaate	tcoctgggagt	gagggagaaa	cagggagctg	1590
5	aatcctcccc	caagctgttc	caggccagag	gactctgcag	tacctttctcc	tacatctagt	1650
	aacaaaagaat	ggtgataacc	atgcactggt	tcaaggttct	ggagttctcc	atgaaacttg	1710
	ggttaatttt	gctcagagta	tccggagtta	gccactaggg	tgcgggtgaa	atgggatgga	1770
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	ctcagggtct	gggttttcaa	cctgtggcga	caggaggcag	ggcagactgt	ggaggacagg	2010
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	<400> 150						
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	ctggcgcgcg	acctgtctaa	gaccagggtc	ctgccaaagcg	ctaggagggcg	gcgtgccagg	180
	ggcgctaggg	aactgcggag	cgcgcgcgcc	atg ggg ccg ccg cct ggg gcc			231
	Met Gly Pro Pro Pro Gly Ala						
30	1 5						
	ggg gtc tcc tgc cgc ggt ggc tgc ggc ttt tcc aga ttg ctg gca tgg						279
	Gly Val Ser Cys Arg Gly Gly Cys Gly Phe Ser Arg Leu Leu Ala Trp						
	10 15 20						
	tgc ttc ctg ctg gcc ctg agt ccg cag gca ccc ggt tcc egg ggg gct						327
35	Cys Phe Leu Leu Ala Leu Ser Pro Gln Ala Pro Gly Ser Arg Gly Ala						

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	25	30	35	
	gaa gca gtg tgg acc gcg tac ctc aac gtg tcc tgg cgg gtt ccg cac			375
	Glu Ala Val Trp Thr Ala Tyr Leu Asn Val Ser Trp Arg Val Pro His			
	40	45	50	55
5	acg gga gtg aac cgt acg gtg tgg gag ctg agc gag gag ggc gtg tac			423
	Thr Gly Val Asn Arg Thr Val Trp Glu Leu Ser Glu Glu Gly Val Tyr			
	60	65	70	
	ggc cag gac tgg ccg ctg gag cct gtg gct ggg gtc ctg gta ccg ccc			471
	Gly Gln Asp Ser Pro Leu Glu Pro Val Ala Gly Val Leu Val Pro Pro			
10	75	80	85	
	gac ggg ccc ggg gcg ett aac gcc tgt aac ccg cac acg aat ttc acg			519
	Asp Gly Pro Gly Ala Leu Asn Ala Cys Asn Pro His Thr Asn Phe Thr			
	90	95	100	
	gtg ccc acg gtt tgg gga agc acc gtg caa gtc tct tgg ttg gcc ctc			567
15	Val Pro Thr Val Trp Gly Ser Thr Val Gln Val Ser Trp Leu Ala Leu			
	105	110	115	
	atc caa cgc ggc ggg ggc tgc acc ttc gca gac aag atc cat ctg gct			615
	Ile Gln Arg Gly Gly Gly Cys Thr Phe Ala Asp Lys Ile His Leu Ala			
	120	125	130	135
20	tat gag aga ggg gcg tct gga gcc gtc atc ttt aac ttc ccc ggg acc			663
	Tyr Glu Arg Gly Ala Ser Gly Ala Val Ile Phe Asn Phe Pro Gly Thr			
	140	145	150	
	cgc aat gag gtc atc ccc atg tct cac ccg ggt gca gta gac att gtt			711
	Arg Asn Glu Val Ile Pro Met Ser His Pro Gly Ala Val Asp Ile Val			
25	155	160	165	
	gca atc atg atc ggc aat ctg aaa ggc aca aaa att ctg caa tct att			759
	Ala Ile Met Ile Gly Asn Leu Lys Gly Thr Lys Ile Leu Gln Ser Ile			
	170	175	180	
	caa aga ggc ata caa gtg aca atg gtc ata gaa gta ggg aaa aaa cat			807
30	Gln Arg Gly Ile Gln Val Thr Met Val Ile Glu Val Gly Lys Lys His			
	185	190	195	
	ggc cct tgg gtg aat cac tat tca att ttt ttc gtt tct gtg tcc ttt			855
	Gly Pro Trp Val Asn His Tyr Ser Ile Phe Phe Val Ser Val Ser Phe			
	200	205	210	215
35	ttt att att acg gcg gca act gtg ggc tat ttt atc ttt tat tct gct			903

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	Phe Ile Ile Thr Ala Ala Thr Val Gly Tyr Phe Ile Phe Tyr Ser Ala	
	220 225 230	
	cga agg cta cgg aat gca aga gct caa agc agg aag cag agg caa tta	951
	Arg Arg Leu Arg Asn Ala Arg Ala Gln Ser Arg Lys Gln Arg Gln Leu	
5	235 240 245	
	aag gca gat gct aaa aaa gct att gga agg ctt caa cta cgc aca ctg	999
	Lys Ala Asp Ala Lys Lys Ala Ile Gly Arg Leu Gln Leu Arg Thr Leu	
	250 255 260	
	aaa caa gga gac aag gaa att ggc cct gat gga gat agt tgt gct gtg	1047
10	Lys Gln Gly Asp Lys Glu Ile Gly Pro Asp Gly Asp Ser Cys Ala Val	
	265 270 275	
	tgc att gaa ttg tat aaa cca aat gat ttg gta cgc atc tta acg tgc	1095
	Cys Ile Glu Leu Tyr Lys Pro Asn Asp Leu Val Arg Ile Leu Thr Cys	
	280 285 290 295	
15	aac cat att ttc cat aag aca tgt gtt gac cca tgg ctg tta gaa cac	1143
	Asn His Ile Phe His Lys Thr Cys Val Asp Pro Trp Leu Leu Glu His	
	300 305 310	
	agg act tgc ccc atg tgc aaa tgt gac ata ctc aaa gct ttg gga att	1191
	Arg Thr Cys Pro Met Cys Lys Cys Asp Ile Leu Lys Ala Leu Gly Ile	
20	315 320 325	
	gag gtg gat gtt gaa gat gga tca gtg tct tta caa gtc cct gta tcc	1239
	Glu Val Asp Val Glu Asp Gly Ser Val Ser Leu Gln Val Pro Val Ser	
	330 335 340	
	aat gaa ata tct aat agt gcc tcc tcc cat gaa gag gat aat cgc agc	1287
25	Asn Glu Ile Ser Asn Ser Ala Ser Ser His Glu Glu Asp Asn Arg Ser	
	345 350 355	
	gag acc gca tca tct gga tat gct tca gta cag gga aca gat gaa ccg	1335
	Glu Thr Ala Ser Ser Gly Tyr Ala Ser Val Gln Gly Thr Asp Glu Pro	
	360 365 370 375	
30	cct ctg gag gaa cac gtg cag tca aca aat gaa agt cta cag ctg gta	1383
	Pro Leu Glu Glu His Val Gln Ser Thr Asn Glu Ser Leu Gln Leu Val	
	380 385 390	
	aac cat gaa gca aat tct gtg gca gtg gat gtt att cct cat gtt gac	1431
	Asn His Glu Ala Asn Ser Val Ala Val Asp Val Ile Pro His Val Asp	
35	395 400 405	

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	aac cca acc ttt gaa gaa gac gaa act cct aat caa gag act gct gtt	1479
	Asn Pro Thr Phe Glu Glu Asp Glu Thr Pro Asn Gln Glu Thr Ala Val	
	410 415 420	
	cga gaa att aaa tct taaaatctgt gtaaatagaa aacttgaacc attagt	1530
5	Arg Glu Ile Lys Ser	
	425	
	aataacagaa ctgccaatca gggcctagtt tctattaata aattggataa atttaataaa	1590
	ataagagtga tactgaaagt gctcagatga ctaattattat gctatagtta aatggcttaa	1650
	aatatttaac ctgttaactt ttttccaaa actcattata atatttttca taggcaagtt	1710
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	ttttcattta taacaatttt ttataaaaa catgttgctt ttaaaatgtg gagtagctgt	1830
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	atgtgtcagg gttttctcc aggtgcttat attgatctgg aattgtaatg taaaagcaa	1950
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25	tcaaattata gcagaattta ggcaaaaaa aaacagacat gtatttttgt ttgctgaatg	2670
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	attgattctc ttttaataata aaatgtaaat aaaatattcc aat	2773